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James C. White

THE BRITISH
JOURNAL OF DERMATOLOGY.

JANUARY–MARCH, 1916.

IN MEMORIAM: JAMES CLARKE WHITE.

By SIR MALCOLM MORRIS, K.C.V.O.

The tidings of the death, in his eighty-third year, of the pioneer of American dermatology has been received with profound regret by dermatologists in these islands. In the Presidental Address to the Section of Dermatology and Syphilography at the Seventeenth International Congress of Medicine, held in London in 1913, I spoke of him as the veteran "leader of those who represent the dermatology of the great nation across the Atlantic which is still 'mewing its mighty youth.'" It is true that two years before that date he resigned his practice into the very capable hands of his son, Dr. Charles J. White, and was spending his well-earned leisure in the intellectual and artistic pursuits of which he had never lost sight during his laborious professional career. But so long as he was living no one else could be thought of as the leader of American dermatology. And now that he has left "this bank and shoal of time," the honourable task has been assigned to me of paying to his memory, however imperfectly, the tribute which British dermatologists feel to be richly due. Many were the opportunities I had of seeing what manner of man he was. Six times he visited Europe; and when I went to Montreal in 1897 to attend the Annual Meeting of the British Medical Association, I enjoyed his hospitality in Boston. A more charming host I have never known. In all relations, indeed, he was a model of cultured and dignified courtesy, and, though the word is going out of vogue, one need not fear to apply to him "the grand old name of gentleman."

As he has told the world in his most readable Reminiscences,* he derived from a good Ulster stock, an ancestor of his, who left London in the year of "the glorious Revolution," being one of the heroes of Londonderry, who, when the siege was raised, was presented with the keys of the city by Governor Walker. In 1725 a son emigrated to America, and one of his direct descendants was the future founder of American dermatology, born at Belfast, Maine, in 1833. He began his college career at Harvard at the age of sixteen. During his course there the teaching staff included Longfellow, the poet, with Asa Gray and Louis Agassiz, the former to become in after years the redoubtable champion of Darwinism against the formidable assaults of the latter; while among the "Overseers" was Daniel Webster, the orator, and George Bancroft, the historian. In his last year there came to him one afternoon in church the "sudden conviction" that medicine was to be his life's work, so, having graduated (1853), he enrolled himself as a medical student. At that time the only hospital available to students was the Massachusetts General Hospital, the amphitheatre of which was still famous as the room where anæsthesia by ether was first performed (1846), and was still furnished with the hooks and staples for the cords which controlled the patients under torture. There he once saw an amputation done upon a patient who refused ætherisation. "A fine-looking old New England farmer," he says, "stood up very erect, held out his bare arm, which was amputated near the shoulder-joint, without moving a muscle or uttering a sound."

It was White's good fortune to learn anatomy under Oliver Wendell Holmes, whose vivacity, wit, ingenuity, and endless fund of stories were all pressed into the service of his teaching. His lectures on physiology were perfunctory, but on his own ground, anatomy, he must have been inimitable. How different was Charles Darwin's experience at Edinburgh, where anatomy was then taught in so lifeless and dreary a fashion that he found it impossible to feel the slightest interest in the subject. White records that at one time Holmes was studying rattlesnakes, a cult which he put to so weird a use in *Elsie Venner*. In the basement he kept a large specimen, and to demonstrate to a friend its power of killing he introduced into the cage a large rat. But instead of waiting to be struck, the rat sprang at the snake and fastened upon its head, and the encounter ended in the snake's head being bitten off, its owner meanwhile dancing about in frantic distress, exclaiming, "Oh, he's killing my snake! Take him off, take him off!"

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* *Sketches from My Life*, 1833–1913. Riverside Press. Cambridge (U.S.A.). 1914.

Another of the professors, Cooke, if he had not Holmes's wit, was evidently not lacking in high spirits. White and another student happened to be present when he asked Holmes to inspect a powerful electric battery which he had just acquired. With a grin, Cooke invited the other student, a man of muscle, to see if he could stand the current, and as soon as the handles had been gripped he turned the current on full power. His unfortunate victim was unable to let the handles go, but with a great oath he "yanked the whole concern out on the laboratory floor." When the professors saw the valuable apparatus a heap of ruins their wicked glee turned to sorrow.

In 1855 White saw Prof. Cooke condense carbonic acid to snow, little thinking what a valuable agent it was to become in dermatological practice. At the close of the winter course of lectures in this year he passed his examinations in all the branches, and received his degree of Doctor of Medicine. Soon afterwards his year of service at the hospital expired, and he spent a couple of months in Prof. Cooke's laboratory working at chemistry, in which he had all along taken a special interest. Not satisfied of his competence to practise medicine, he decided to spend a year at Vienna, whose medical school, with such teachers as Hebra, Rokitansky, Hyrtl, Oppolzer, and Skoda, was then the most famous in the world.

As he passed up the English Channel and through the Straits of Dover he caught glimpses of England, and everything he saw, as he records, "seemed almost like home." He reached Vienna early in September (1856). During his stay in this city he never had more than four or five American fellow-students, and he was the first American student to spend a whole year there. But the renown of the Medical School of Vienna had continued to grow, and when I was studying there, fifteen years later, the few had become many.

White's graphic sketches of the professors are absorbingly interesting to all who knew the men he describes. Of Hebra, "the founder of the modern school of dermatology," as he terms him, he writes with the greatest enthusiasm. "He was an admirable teacher," he says, "and no one could forget his clear and convincing method of presenting a subject, and the exhaustive use of his abundant clinical material for instruction in diagnosis and therapeutics. It was a perfect system of object teaching given by a master of the keenest observation." Many years afterwards, when his own professional career was drawing towards its close, he declared that he still believed Hebra's teaching was "unparalleled," an estimation in which I fully concur.

While closely following Hebra's lectures, he did not fail to acquire much valuable knowledge in other branches of medicine, and on one occasion at least he found an opening for imparting a little instruction. Heller, the Professor of Chemistry, in drawing attention to some urinary crystals of dumb-bell formation in the field of the microscope, pronounced them to be phosphate of lime. White had the courage to say that he believed they were oxalate of lime, and suggested the application of reagents which would determine the point. The result showed that he was right, and Heller had to endure the rallying of Oppolzer that a young American should have come to Vienna to teach him chemistry.

Nor did White fail to turn to good account his artistic and social opportunities. He revelled in Vienna's delicious music, he went to public balls, he saw something of the clubs, he delighted in the glittering shops, he had the *entrée* of the best American society. From the wife of the Secretary of the American Legation, Mrs. Lippitt, a Viennese who had known Beethoven well and was herself an accomplished pianist, he heard of an incident which brings the composer into association with our own Nelson, and which, so far as I know, is not related in the biographies of either. The majestic Funeral March on the death of a hero which comes into one of the sonatas *(op. 26)* was written, she told him, in commemoration of Nelson when a report reached Vienna that the "shaker of the Baltic and the Nile" was dead. The news proving to be false, Beethoven sent the piece to Nelson, who gracefully replied that it had been a pity to have died before hearing so beautiful a composition.

His crowded and profitable year in Vienna ended, White returned to America by way of Paris and London, seeing something of the schools of medicine and of the hospitals in both those cities. He began to practise at Boston towards the end of 1857. He did not at once specialise in dermatology. In the following year he was appointed teacher of chemistry in the Medical School, and in 1866 was made adjunct professor; but when his term of office expired with the resignation of his chief he decided not to go further in this direction. By that time he had become Visiting Physician to the Massachusetts General Hospital, and his private practice, especially in skin-diseases, had become considerable. In 1871 he was appointed Professor of Dermatology, a new chair in the Medical School, and the first to be established in the States. The year before this an out-patients' department for skin-diseases had been created at the hospital and placed in his charge, and he held the post for three-and-thirty years.

An incident that occurred early in his professional career must not be passed without notice. A patient of his died of acute pulmonary tuberculosis soon after he had successfully treated her for chronic eczema, and in the fashionable circle in which she had moved he was reflected upon as the indirect cause of the fatal disease. Hearing of this, the venerable Dr. James Jackson went out of his way to assure the family that the notion that the healing of a skin-disease sometimes led to the development of a more serious latent affection was the merest superstition. White never forgot this act of kindness, and testifies that in his career in the Medical School he often felt it an inspiration to occupy the chair in which his generous defender had sat long before.

In the words of the *Boston Medical and Surgical Journal,* applied to White, "courage and determination" were required to practise dermatology as a speciality in those days, when "Damn all specialists!" was a favourite anathema in the mouths of well-known city physicians, profoundedly convinced of their own omniscience. In 1907, looking back to the beginning of his career as a dermatologist, he declared that it had been "a long and hard struggle to overcome the opposition, on the part of the general profession, the governing boards of hospitals, and the faculties of our medical schools, to the position of dermatology as an independent department of medicine." This is an utterance which appeals to the sentiment of fellow-feeling in dermatologists on this side. I may be pardoned for recalling that when I was considering the question of cultivating dermatology as a speciality I sought the advice of one of the most eminent surgeons and teachers in London, who frankly, and I am sure disinterestedly, did his best to dissuade me from the enterprise. In the United States the struggle had to be made "single-handed in every hospital and every institution for medical education," and even so late as 1907 the opposition had not been wholly overcome. It has been much the same in this country, and here, as there, time has been on the side of those who were sensible of the need for devoting all the resources of their minds to the study and practice of a branch of medicine which, though primarily concerned with the surface of the body, is not precisely free from complexity and obscurity.

Judicial and temperate as was his cast of mind, and free as he was from rancorous feeling, White was a good fighter, and one may hope, for his own sake, that he was no stranger to the joy of battle. He did much more than lead the movement in America for the recognition of dermatology; he was also one of the protagonists in the great conflict for the reform of American medical education generally. This is not the place to enter in detail into that phase of his work; but it is easy to see how much need there was for reform when one knows that White's examination in surgery at graduation consisted in the question: "Well, White, what would you do for a wart?" That and nothing more!

In passing, one may note with surprise that among those whose opposition White had to encounter was Oliver Wendell Holmes, who was perhaps inhibited from being on the side of the angels this once by the strain of idealistic conservatism, which may be seen in his delectable reflective writings. It is pleasant to know that Emerson was on the right side in the great controversy. After White had delivered his memorable address of 1870 on the reform of medical education, Emerson called upon him to shake hands with the man who had "made the feathers fly," and told him that the address had "stirred him like a trumpet." This was praise indeed.

Under White's sagacious guidance, and with the active co-operation of such colleagues as Duhring, Nevins Hyde, and Prince Morrow—to name only those who have passed away—the progress of dermatology in America was rapid. In 1877, in his Presidential Address at the first annual meeting of the American Dermatological

Association, he was able to speak of the advance that had been made since he began to practise his speciality. Twenty years later (1897) it again fell to him to deliver the Presidential Address, and now he had a much more remarkable story of progress to tell. Ten years after this (1907) he gave the Presidential Address at the Sixth International Dermatological Congress, held in New York. "We have one hundred and twenty-five professors and teachers of dermatology," he could now tell his colleagues from other lands. "We have large and well-equipped special laboratories and clinics, perhaps the largest and most magnificent medical school building in the world, and we have produced some admirable and exhaustive treatises and countless papers on dermatology. Most of our teachers have had the advantage of studying our subject with the most distinguished teachers of Europe, living and dead." You see, therefore, he was able in no boasting mood to claim, "that you should find us very much as yourselves, and that we meet as equals." Even now, however, he had to own that only "a few" of the large hospitals had wards for the exclusive reception of skin-diseases. In these islands also there is still great scope for improvement in the same direction, for while some ground has been gained, there is much more to be won before British dermatology can profess to be satisfied.

The list of White's writings occupies eighteen pages of his book; it includes 125 medical papers, 50 reviews, 94 editorials, 15 translations, 22 papers on natural history, and eight "books and chapters," one of the books being that on "Dermatitis Venenata." To leprosy, much more frequent in America than in this country, he gave a good deal of attention; but there were few dermatoses upon which he did not write, and he wrote on nothing which he did not illuminate. At the International Dermatological Congress in Paris in 1889 he described a new affection which he termed Dermatitis follicularis, and which had just been observed independently by Darier, who styled it vegetating follicular psorospermosis; it is now more generally known as Keratosis follicularis, a name which White himself afterwards adopted.

Much as he did for the advancement and enrichment of his own branch of medicine, White was a great deal more than a specialist in cutaneous affections, nor can it be doubted that his dermatology was the gainer from the variousness and breadth of his knowledge. He had an exceptional grasp of medical theory, he was an expert in natural history, a man of wide general reading, and a collector of porcelain and antique furniture. Space fails to enumerate all the learned and professional societies in which he at one time or another held office; but it may be noted that he served the Boston Society of Natural History as Curator of Comparative Anatomy, arranged the great La Fresnaye ornithological collection, and formed an extensive herbarium of his own; that from 1866 onwards he was a member of the American Academy of Arts and Science; and that the dermatological societies of all the great capitals, including London, were proud to admit him to their ranks as an honorary or a corresponding member.

The very brief concluding chapter of his reminiscences may be regarded as his swan-song. "Thus," he wrote at the end of 1913, "I have lived my eighty years—years of childhood, pleasant and simple, in Maine; of dawning manhood, under distinguished and inspiring teachers at Harvard, in earnest and devoted study of medicine at home and abroad; long years of professional work in the study of and in efforts to cure disease, and in imparting such knowledge to other men." He goes on to say that he had taken much outdoor exercise, mostly in the form of walking, had always enjoyed good health, liked good food and good wine, although he had never drunk wine habitually and had abstained entirely from spirits and malt liquors and tobacco, and that, while a constant and hard worker, he had found time for social pleasures, for the reading of many books of many kinds, and, in later life, for travel. "Now," he adds, "I spend my summers on the loveliest island in the Gulf of Maine and my winters with my family and friends in Boston. I am contented with my past and my present." Could anything be more simple and sincere, or more suggestive of a "serene and bright" old age?

CLINICAL NOTE.

From the University's Dermatological Clinic at the Rigshospital in Copenhagen (Director: Dr. C. Rasch).

SECONDARY LICHENOID TRICHOPHYTIDES IN ASSOCIATION WITH KERION CELSI (LICHEN SPINULOSUS TRICHOPHYTICUS).

By C. RASCH.

(Translated from the Danish by W. Jenkins Oliver.)

The two cases which form the subject of this communication are the following:

Case 1.—A boy, aged 13 years, was admitted on October 26th, 1915, to the University's Dermatological clinic at the Rigshospital in Copenhagen with a large kerion of the scalp, in addition to which there were two smaller and flat tinea lesions on the back of the neck and on the upper part of the back, with a third lesion of about the size of a half-crown piece over the left scapula. Microscopical examination of the hairs from these lesions showed much fungus, but cultures of the same were not successful.

On October 29th, *i.e.* fourteen days after the commencement of the affection, there appeared on the back and chest a dense eruption of numerous very small follicular papules of a pale reddish colour. These were not grouped but were diffusely spread, the greatest amount being on the central part of the chest and back, with a smaller number on the arms and only a few on the face. The papules were firm and "horny" to touch, but did not show any bristles or spines.

On November 3rd the boy developed scarlet fever, for which reason he had to be removed from the clinic.

Case 2.—A girl, aged 12 years, who was admitted to the Dermatological Clinic of the Rigshospital on September 17th, 1915, with a large kerion of the scalp, which had been present for some three or four weeks. On October 13th there was first noticed on the back, chest, arms and legs an eruption which consisted of many densely placed miliary papules occurring chiefly in groups, which for the most part were not sharply differentiated from each other. The papules were white, pink or the colour of the skin, very hard and almost "horny" to touch. On many of them was a small bristle or spine of a few millimetres length. These spines could be removed by traction when there appeared a small cavity in the skin. No fungus was found in them on microscopical examination. The eruption was present in greatest amount on the back and chest, which afterwards became completely covered (Figs. 1 and 2), and extended to a smaller degree on to the arms and downwards on to the legs. The hands and feet were quite clear, while only a few discrete papules occurred on the face.

While the kerion lesion, treated with fomentations, became healed by the middle of November, the condition on the back and chest, as described, continued to spread, so that the whole trunk was eventually covered by the eruption. Now and again there was considerable irritation, with the result that the patient by scratching loosened a large number of the white spines, so that the amount of these varied considerably from time to time during this period. Eventually, towards the end of November, there were many of these spines or bristles, and the numerous horny papules gave to the hairs the appearance of a grater, like that seen in Pityriasis rubra pilaris. On December 1st all the horny papules had disappeared, while there still persisted many of the delicate white bristles.

I can only look upon these two cases in both their dermatological and general pathological aspects as typical examples of that very remarkable affection which has been called "Lichenoid trichophytide," and which was first described by Jadassohn in the autumn of 1911 during the discussion on Bloch's discourse on ringworm at the Swiss Medical Congress on October 29th, 1911. Jadassohn said as follows (*Autoreferat i Correspondenz—Blatt. f. Schweizer Aerzte*, 1912, p. 24): "With Kerion Celsi, especially about the time of healing, he had often seen occurring, either in groups or diffusely spread, an eruption which consisted of small pale follicular nodules, sometimes very numerous, at other times in lesser numbers, which after some time disappeared. They most closely resembled Lichen scrofulosorum, but did not react to tuberculin injections and were also histologically different from this disease. Occasionally they showed small horny spikes or spines, and the condition might then be said to correspond to the picture of Lichen spinulosus." Jadassohn was convinced

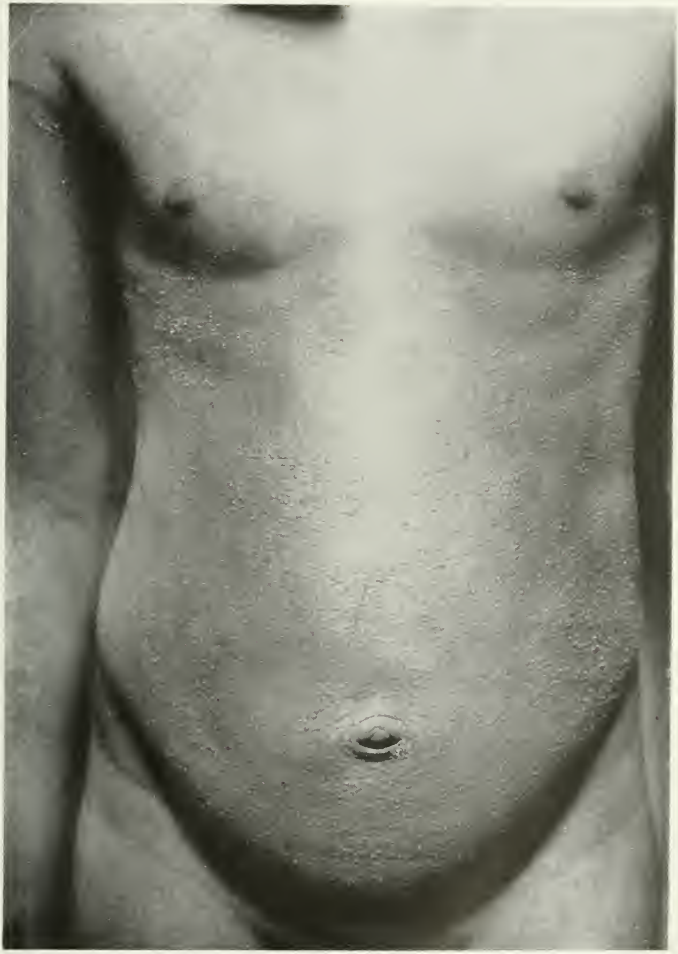

FIG. 1.

TO ILLUSTRATE DR. C. RASCH'S PAPER ON LICHENOID TRICHOPHYTIDES.

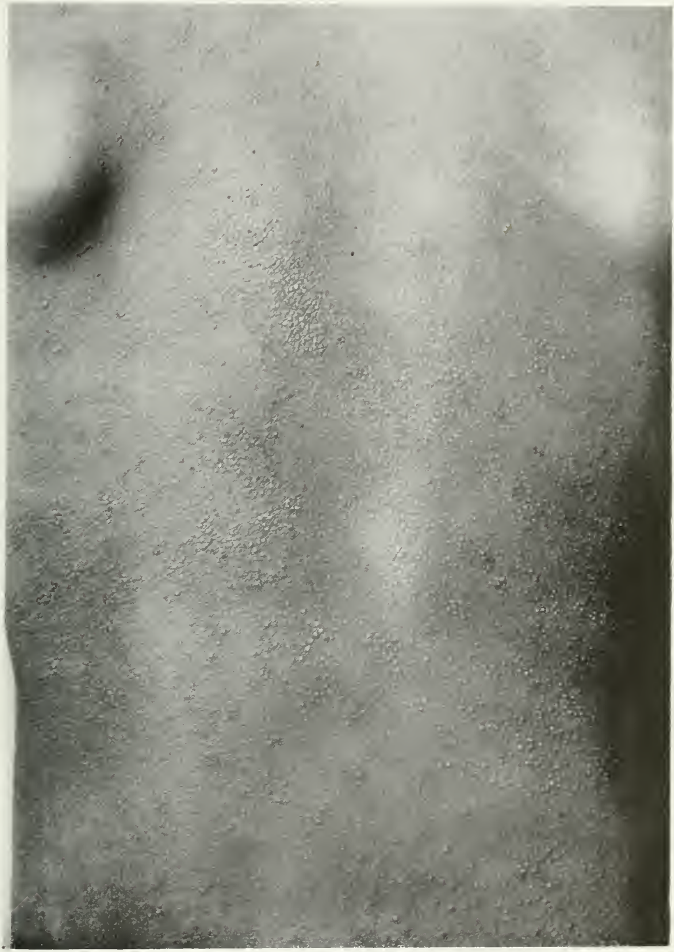

FIG. 2.

TO ILLUSTRATE DR. C. RASCH'S PAPER ON LICHENOID TRICHOPHYTIDES.

that the only case of Lichen spinulosus which he had seen (published by Lewandowsky in 1905) was of such a tinea form. Since also this child had a Kerion Celsi, Jadassohn was inclined to hold the opinion that these eruptions, in association with deep-seated tinea, must be founded upon exogenous auto-intoxications. Two years later (1913) B. Bloch, of Basle (*Die allgemein-pathologische Bedeutung der Dermatomykosen,* Halle, 1913, p. 82) reported a case of the same nature in a boy with kerion due to a trichophyton of the gypseum group. This patient had also an extensive outbreak on both legs of several nodules which resembled Erythema nodosum, and which Bloch also is inclined to bring into ætiological relation with Kerion Celsi. Of the lichenoid form Bloch had seen many cases and was of the opinion that they, like Lichen scrofulorosum, must arise by a hæmatogenous route.

In March, 1914, Arthur Guth, of Zurich, one of Jadassohn's former assistants, reported fifteen cases of "Lichenoid trichophytide," all from the clinic in Berne ("Ueber lichenoid (klein-papulöse, spinulöse) Trichophytie," *Arch. f. Derm. u. Syph.,* Bd. 118, p. 856). Of these cases, fourteen were in children and one in an adult with a deep-seated ringworm of the beard. The condition appears to be very common, since Guth states that nearly all children with kerion show it to a greater or smaller degree. It appears either when the kerion is at its most acute stage or when it is about to fade away, and is not as a rule accompanied by subjective symptoms. The rash may either appear somewhat suddenly at one time or can extend by repeated outbreaks. It varies greatly in regard to its extent, duration, and appearance, being found in greatest amount on the body, to a lesser extent on the limbs, and only in a few cases on the face. The number of the individual lesions is very variable, as these are sometimes very few, while at other times they are very numerous. They may be either diffusely spread, or be grouped, or both the one and the other. Their duration is very variable; sometimes they may vanish in the course of a few days, or, again, they may last for several weeks. In the second of my cases the eruption was at its greatest extent and intensity five weeks after the kerion had disappeared, and is still present.

In the majority of cases the eruption consists of miliary follicular pale or pink, pointed or flat papules, which sometimes have on the summit a small scale or crust, or more rarely small vesicles or pustules. When they are about to disappear, they may develop a quite small scale. In only one single case was there left light brownish pigmentation.

In some cases there may develop white bristles or spines on a few or many of the papules (Lichen spinulosus). In addition to this lichenoid form, Guth has also seen in one patient with kerion an eruption which suggested Pityriasis rosea, and which did not show any fungus on either microscopical or on cultural investigation.

Histologically the condition appears, according to Lewandowsky's and Guth's investigations, as a follicular or perifollicular inflammation. The follicle is more or less dilated, being filled with a mixture of round and epithelial cells. In the spinous form there is some considerable parakeratosis in the wall of the follicle, and the horny layers in connection with it are pushed out of the follicle by the pressure inside, so giving rise to the development of a bristle or spine.

The diagnosis will, as a rule, be easy for anyone who knows of this disease. The condition with which it may most readily be confounded is Lichen scrofulorosum. This latter disease, however, is as a rule more limited, and the lesions are more grouped and of a darker, bluish-red colour. They have much less tendency to develop spines, and their evolution is much slower. While in association with the "Lichenoid trichophytides" there is found a kerion lesion or the remains of such, with Lichen scrofulorosum other signs of tuberculosis are usually present and the affection reacts to tuberculin injections.

With regard to the differential diagnosis from Lichen spinulosus, I am of the opinion that some of the cases previously described under this name are probably identical with the "Lichenoid trichophytides," while others, such as Adamson's case (*Brit. Journ. Derm.*, February, March, 1905), are different. This question should be reconsidered by paying particular attention in the investigation of each case to the presence of an existing or preceding kerion. The affection may in a high degree resemble Pityriasis rubra pilaris, which sometimes also shows spiny lesions, but which in children is nearly always accompanied by typical redness and scaling of the face, soles and palms, and is besides of a much more chronic nature.

With regard to pathogenesis, one has to consider either a multiple exogenous inoculation or an hæmatogenous infection by either the

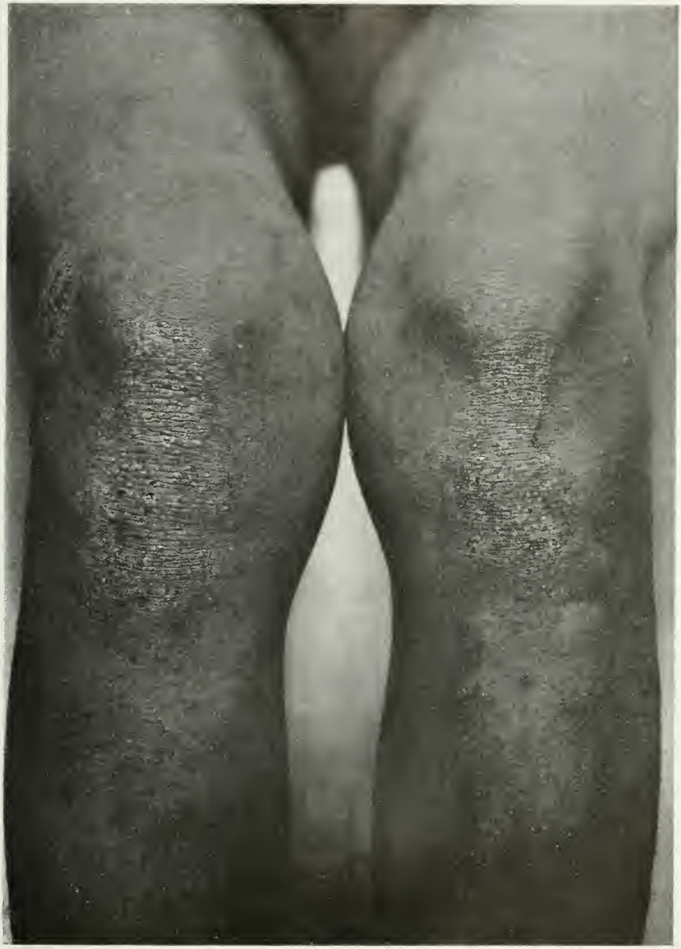

FIG. 3.

TO ILLUSTRATE DR. C. RASCH'S PAPER ON LICHENOID TRICHOPHYTIDES.

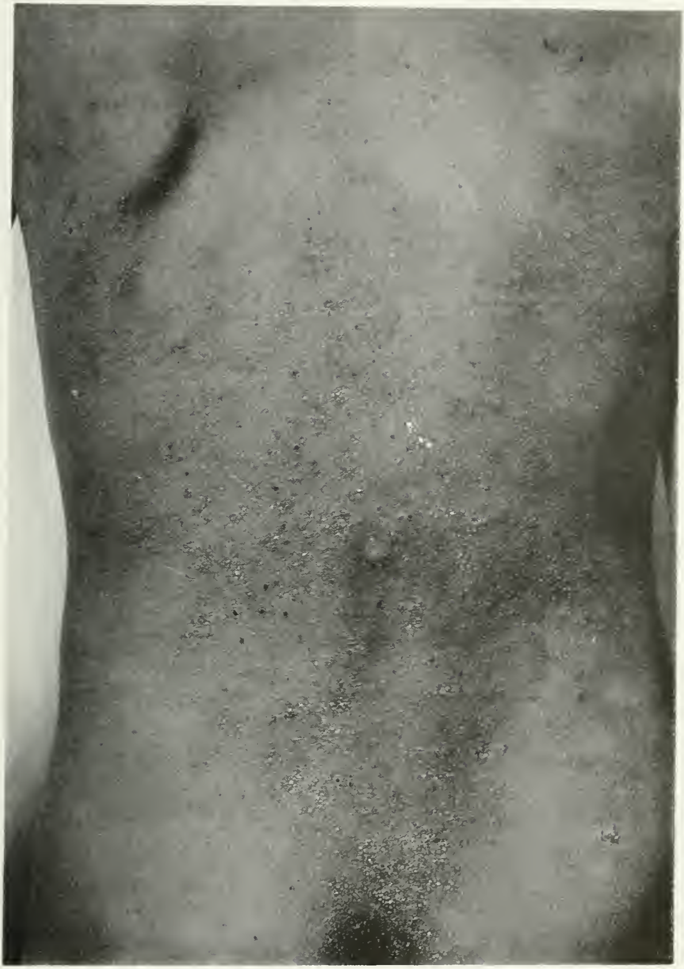

Fig. 4.

TO ILLUSTRATE DR. C. RASCH'S PAPER ON LICHENOID TRICHOPHYTIDES.

fungus itself or by its toxins. For my part I am most inclined to believe that the condition has an internal toxic origin. Jadassohn, in 1911, considered an exogenous inoculation as being the more probable. However no fungus is found in the lesions (only Guth has on one occasion found a single mycelial thread) which by their diffuse, indeed in some cases almost generalised exanthematic appearance, certainly point to some internal agent as being the cause of the affection. B. Bloch also supposes that the condition has an internal toxic origin.

(My two cases of Lichenoid trichophytides were demonstrated before the Danish Dermatological Society in November, 1915.)

I have, since the above was written, seen two more cases of very extensive trichophytides in children with kerion. In one of these (Figs. 3 and 4) there developed extremely numerous minute psoriasiform scales on the papules.

(Note.—Since this article was written I have obtained a culture of Trichophyton faviforme from a sister of Case 2, who also suffered from kerion and lichenoid trichophytides.)

TWO CASES OF HERPES ZOSTER ASSOCIATED WITH A GENERALISED ERUPTION OF VARICELLA-LIKE SPOTS: ONE OF THE CASES FOLLOWED BY OCULOMOTOR PARESIS, MYDRIASIS, AND FRONTAL ANÆSTHESIA.

With a Short Analysis of the Literature of the Subject and Remarks on the Ætiology of Herpes Zoster.

By F. PARKES WEBER, M.D., F.R.C.P.

First Case.

The patient, A. H—, Jewish, male, aged 59 years, was admitted to hospital on October 30th, 1915, suffering from chronic lymphatic leukæmia, with considerable enlargement of the cervical, axillary and inguinal lymphatic glands, and moderate enlargement of the spleen and liver. The glandular enlargement had commenced gradually some six years ago, and about one and a half years ago the patient had suffered from malaria in Palestine. Roentgen-ray examination of the thorax (Dr. James Metcalfe) showed masses of enlarged lymphatic glands at each side of the great vessels above the heart and in the mediastinum. Blood-examination (November 1st, 1915): hæmoglobin, 60 per cent.; red cells 3,200,000 and white cells 53,600 to the c.mm. of blood. Of the white cells 97 per cent. were small lymphocytes. The red cells showed slight poikilocytosis, polychromatophilia, and anisocytosis. No nucleated red cells were seen. The Wassermann reaction (Dr. Hans Schmidt) was negative. Treatment with arsacetin was commenced on November 6th, 1915, and two weeks later an eruption of typical Herpes zoster of the right shoulder broke out (connected doubtless with the arsenical therapy), which was accompanied by a good deal of pain. About five days later a generalised but scanty eruption of varicella-like spots occurred. These spots were scattered about the trunk, and gradually disappeared without causing any trouble, whereas the patches of the Herpes zoster proper dried up, leaving depressed scars covered with dark scabs. Early in December, however, the patient was apparently free from any pain connected with the Herpes zoster, though he complained of other pains lower down in the back.

The patient left the hospital on December 13th, 1915, and (in connection with the remarks I shall make further on) it is perhaps just worth mentioning (though doubtless a mere coincidence) that a little boy, aged 4 years, who was in the same ward with the patient, but was discharged on December 3rd, 1915, developed varicella, I was told, ten days later at his own home—that is to say, ten days after leaving my patient with Herpes zoster.

Second Case.

The patient was an elderly widow, about 60 years of age, who, during the last week of August and the first two weeks of September, 1915, suffered from neuralgia of the left side of the head in the occipital region and in the area of the distribution of the first branch of the fifth cranial nerve, particularly nasal and supra-orbital neuralgia. She likewise complained of slight general malaise. Then (September, 1915) an eruption of typical Herpes zoster appeared on the forehead, and this soon extended over the whole of the left half of the forehead, the left temple and front part of the hairy scalp to the middle line, involving also the upper eyelid, the left half of the nose, and the outer part of the margin of the left lower eyelid. The pain continued very severe. The herpetic eruption soon became confluent and partly hæmorrhagic. There was much œdema of the whole face, particularly of the left half. The pre-auricular lymphatic glands and those along the anterior border of the sternomastoid muscle were much enlarged and very tender. At the end of the first week of the typical Herpes zoster affection a generalised vesicular eruption of small varicella-like spots was noticed, scattered over the trunk and extremities; two spots were situated near the outer margin of the right orbit, about six were on the lower extremities, and about twenty were on the chest. This generalised vesicular eruption was not accompanied by any subjective symptoms, and the spots disappeared gradually in the course of two weeks. The true Herpes zoster eruption, on the other hand, took two months to dry up; by the end of that time the scabs had largely disappeared.

About six weeks after the onset of the Herpes zoster, when the patient began to keep her left eye open again, she complained of diplopia, and this, on examination, was found to be due to paresis of the left rectus superior muscle. The diplopia disappeared about three weeks later.

The eyeball was considerably injected throughout the illness and there was much lacrymation, with a good deal of muco-purulent discharge from the conjunctiva. The cornea, apart from some slight marginal erosions, remained free from ulceration and infiltration. Sensation in the cornea and bulb was distinctly impaired. The eye was kept under atropine.

The condition on December 10th, 1915, that is to say, about three months after the commencement of the illness, was as follows. There was very severe neuralgia in the left eye, the left temple and side of the head, and the left half of the forehead; also in the region of the orbital branch of the second division of the fifth nerve (that region was distinctly hypersensitive to touch). There was cutaneous anæsthesia (to touch and pressure) of the left half of the forehead and the upper eyelid. There was cutaneous hypo-æsthesia of the left front portion of the scalp up to the middle line. The upper eyelid was still red and somewhat thickened. There was moderate lacrymation. The pupil (two weeks after discontinuing the use of atropine) was still somewhat dilated and reacted sluggishly to light. There was still a little œdema of the left cheek. The eyeball was slightly injected, but there was hardly any excess of the conjunctival secretion. There was much scarring of the left half of the forehead. The conjunctival sensation was purposely not tested.

During the second week of January, 1916, the left pupil became normal again in regard both to its size and its reactions. To-day (February 18th, 1916) I hear that, except for the pupil, the condition is much the same as noted on December 10th, 1915. There is some chloasma-like pigmentation of the left cheek. The neuralgia and anæsthesia remain. A slight improvement followed treatment with eight intra-muscular injections of "Tiodine," but that course of treatment had to be discontinued on account of exacerbations of old chronic bronchitic troubles, with rise of temperature (up to 102° F.), lasting for two days or so at a time. On one occasion a scarlatiniform eruption appeared on the patient's trunk and lasted about two days.

I am indebted for the notes of the second case to my colleague, Dr. Charles Markus, through whose kindness I saw the patient.

Remarks.*

The Generalised Eruption, and the Question of the Ætiology of Herpes Zoster.

Many cases of Herpes zoster associated with or followed by a generalised vesicular eruption have been described (*cf.* references Nos. 1 to 20), mostly under the heading *Herpes zoster generalisatus.* Minet and Leclercq (14), who collected twenty-five cases, say that the generalised eruption may break out simultaneously with, or from a few hours to a few days after, the typical Herpes zoster. A case published by Fischl (19) was in a patient with lymphatic leukæmia; and lymphatic leukæmia was present likewise in the first case of the present paper. Several of the recorded cases of Herpes zoster generalisatus have been in elderly persons (for instance, references 6, 13, 15, 17). In the recent account of a case of generalised Herpes zoster in a man, aged 80 years, G. Pernet (18) writes that in Herpes zoster "it is well known, since Tenneson (1) called attention to the point, that here and there aberrant vesicles may usually be found if carefully looked for, but in this case there were a very large number of discrete vesicles scattered all over the trunk and limbs, very few being found, however, below the knees. . . . There were also a few about the face and scalp, but none in the mouth. The generalised vesicular rash looked like a bad attack of varicella."

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* The figures in brackets are the numbers of the references to the literature and notes at the end of the paper.

It has been suggested that Herpes zoster is a modified and localised form of varicella (21 to 29). This suggestion would explain likewise the occasional evidence of contagion in Herpes zoster (30 to 35, and 22).

Johann von Bokay (21), at the 16th International Medical Congress, in 1909, published nine interesting observations. In 1888 he examined a child who developed typical varicella ten days after an eruption of thoracic Herpes zoster in another child in the same family. His eight other similar observations were made during the following twenty-one years, and in each of them typical varicella was observed to break out in a patient (in one instance an adult patient) eight to twenty days after exposure to typical Herpes zoster. In three of the observations the Herpes zoster was followed by respectively two, three, and four cases of varicella. In none of the cases was there any evidence of exposure to ordinary varicella.

Paul Heim (22) records a similar observation of his own. A mother suffered from typical thoracic Herpes zoster, and the only one of her children who was at home when the eruption broke out developed typical varicella ten days later. Four days after the commencement of the mother's eruption another of her children came home and developed typical varicella twelve days later—that is to say, six days after the first child. The varicella eruption was much more severe in the second child. In the right axillary region the vesicles were smaller than elsewhere and had a zoster-like grouping, and the child complained of pain there. J. von Bokay had also observed that general varicella eruptions may sometimes show local zoster-like grouping of the vesicles, and he had quoted confirmatory evidence from the writings of earlier authors. Heim suggests that the unknown microbe of varicella may, under certain as yet unknown conditions, give rise to a localised eruption resembling

Herpes zoster, and that this again may further give rise to a varicella-like eruption. He adds that in May, 1912, together with an epidemic of varicella at Budapest, there was evidently a kind of epidemic of Herpes zoster, for during that period, in his hospital and private practice, he observed more cases of Herpes zoster than he had ever observed before in the same time.

Hepworth (27) records a case of Herpes zoster in a mother being followed by varicella in her son after sixteen days interval. Howard Distin (29) tells of a severe attack of Herpes zoster in a father, followed, after twenty-two days, by varicella in his daughter, aged 5 years, though she had apparently not been exposed to any known source of infection. W. P. Le Feuvre (23) gives similar examples observed by himself and by various other medical writers. Instances of varicella being followed by cases of Herpes zoster have likewise been recorded (23 to 26). References to many publications bearing on this alleged connection between Herpes zoster and varicella are given in the References and Notes at the end of this paper (Nos. 21 to 29).

That real Herpes zoster is due to the same (unknown) cause or morbid agent as varicella appears to me extremely improbable. *In the first place,* if that were so, one would expect, during epidemics of varicella, to meet *fairly frequently* with children suffering from typical Herpes zoster, and not merely presenting local zoster-like groupings of varicella vesicles, such as has been alluded to by von Bokay (21), Heim (22), etc. Furthermore, during epidemics of varicella, one would expect to find Herpes zoster in children at the same time as, or preceding, an eruption of varicella, but one does not do so. Since typical eruptions of Herpes zoster do occur in children, one cannot (in terms of the theory in question) explain away the difficulty by supposing that children are not liable to that "modified form of varicella" which (according to the theory in question) *manifests itself in the guise of* Herpes zoster. *In the second place,* the eruption of Herpes zoster in my above-described leukæmia case (A. H.) seemed obviously to have been excited by the arsenical treatment employed, and though the Herpes zoster was associated with a slight generalised eruption of varicella-like spots, it would be a very far-fetched explanation to suppose that a varicella-infection was present and played any part in the causation of either eruption. So also in a boy, Roger S—, aged 8 years, to whose case I have alluded elsewhere (36), an eruption of typical Herpes zoster occurred on the right side of the chest, apparently as a result of arsenical treatment for Hodgkin's disease, and this Herpes zoster was accompanied by a generalised vesicular eruption on the trunk. [Such cases remind one, by the way, that Dermatitis herpetiformis has been reported to have followed the use of arsenic.]

It seems to me, however, that cases (see further on) of Herpes zoster may really be of an [as yet unknown] microbic origin, and this would explain the occasional almost epidemic-like frequency of the disease [Paul Heim (22), Kaposi (30), and other writers (31 to 33)], and the examples of apparent contagion of the disease from one patient to another, for instance, the examples collected by Solon Veras (34), the observation of J. Galippe (35), etc. The ordinary sporadic cases of Herpes zoster might then be compared to the ordinary sporadic cases of certain infectious diseases of the nervous system, namely, acute anterior poliomyelitis or polio-encephalomyelitis (the "Heine-Medin disease") and cerebro-spinal meningitis.

If we assume, according to the writings of Head and Campbell (37), von Bärensprung (38), Boeck (39), Sattler (40), Magnus (41), Scheel (42), de Besche (43), André-Thomas and Henyer (44), Anton Sunde (45), and others, that typical Herpes zoster is due to an inflammatory or leukæmic (*cf.* reference 19) or other change in the posterior root ganglia of spinal nerves, or in the ganglia connected with sensory cranial nerves, it is tempting to suppose that, when the herpetic eruption is accompanied by much local disturbance of sensation [especially by pain or anæsthesia], the inflammation has spread or "overflowed" along the sensory roots into the gray substance (*cf.* reference 46) of the posterior horns ("poliomyelitis posterior"), or into the corresponding gray substance of the mesencephalon. Similarly, when the Herpes zoster is accompanied by local muscular paralysis and muscular atrophy, one might suspect that the inflammation has further spread or "overflowed" so as to involve the gray matter of the anterior horns, that is to say, the motor origins of spinal nerves ("poliomyelitis anterior") or the analogous roots of motor cranial nerves. (On these questions compare references 53 to 58 and 40 and 41, especially the notes given in my former paper, reference 53.) It would be quite conceivable that both the exact initial position (focus) and initial extent of the inflammatory or other lesion might vary much in different cases, and such a supposition would serve to explain the supposed occurrence of cases of *Herpes zoster sine herpete,* the attack of Herpes zoster being represented, not by an herpetic eruption, but by neuralgic pain, and possibly by some kind of paralytic or paretic nervous disturbance.

In regard to the further question of whether Herpes zoster may be due to the lately discovered microbic cause of acute anterior poliomyelitis (" Heine-Medin disease "), it is interesting to note that F. E. Batten (47) has seen a vesicular rash in the latter disease resembling diffuse herpes. He writes that the occurrence of herpes in relation to poliomyelitis is well recognised, but he adds : " It is curious how seldom a true herpes is seen in a case of poliomyelitis." (*Cf.* reference 48.)

If Herpes zoster be really due to the same microbic cause as acute anterior poliomyelitis, how can one explain the now acknowledged (and in my limited experience not exceedingly rare) effect of arsenic in inducing an attack of Herpes zoster (*cf.* references 49 to 51, and 36). [In regard to the possibility of Herpes zoster resulting from carbon-monoxide poisoning, *cf.* references 40 and 52.] I have above alluded to two cases (the first case of this paper and case No. 2 in reference 36) in which arsenical medication induced not only an attack of Herpes zoster, but likewise a generalised varicella-like or vesicular eruption. An attack of generalised Herpes zoster has likewise been recorded by Fischl (19) in a patient suffering from lymphatic leukæmia, but, unfortunately, it is not stated whether the patient was under arsenical treatment when the Herpes zoster broke out.

It is, of course, permissible to entertain the idea that a powerful drug like arsenic may, in the case of some individuals, predispose to an infectious disease (Herpes zoster ?). This I have myself ventured to suggest in regard to pneumonia, because I have observed the occurrence of a kind of pneumonia in various patients whilst under treatment with arsenic (36). Nielsen (49) thinks that there can be no doubt as to the fact that arsenic predisposes to Herpes zoster—but he says that the Herpes zoster from arsenic seems to be of the ordinary type—and that no fresh attack occurs if the arsenical medication is continued.

The Ophthalmoplegic Complications and Frontal Anæsthesia.

In a recent paper on a case of "Herpes Zoster with Paralysis of Arm" (53) I gave references to various cases of Herpes zoster associated with muscular paresis, muscular atrophy, and unusual sensory disorders, including many cephalic cases in which ophthalmic, otic, facial, or occipito-cervical Herpes zoster was accompanied by oculomotor or facial paralysis or paresis, sometimes by paralytic mydriasis, and sometimes by disorders of the special senses of smelling, hearing, and tasting. In that paper, however, I unfortunately omitted to refer to the striking cases of H. Sattler (40), Magnus (41), and A. Jaehne (54). The numerous references to the literature given by Wilbrand and Saenger (55) should specially be consulted, as well as the writings of J. R. Hunt (56) and Norman Sharpe (57), in connection with the second case of my present paper. This case is remarkable not only for the severity of the actual herpetic eruption (the *Zoster ophthalmicus seu frontalis*), but for its being followed by frontal anæsthesia and by both external and internal ophthalmoplegic symptoms—namely, paresis of the superior rectus muscle and paralytic dilatation of the pupil. In regard to the dilatation of the pupil, we may mention that C. Achard and J. Castaigne (58), in an article on Cephalic Zona ("Herpes Zoster of the Cephalic Extremity"), described a case in which permanent paralytic dilatation of the left pupil followed an attack of left-sided ophthalmic Herpes zoster, and referred likewise to two other cases in which (permanent or chronic) paralytic mydriasis of one pupil followed ophthalmic Herpes zoster of the same side.

The changes which have been found in cephalic cases of Herpes zoster confirm the work of Head and Campbell (37). Thus André-Thomas and Henyer (44), in a case of ophthalmic Herpes zoster, found changes in the Gasserian ganglion. In a patient who died three days after an eruption of ophthalmic (frontal) Herpes zoster, Sunde (45) found recent, partly hæmorrhagic, partly sero-purulent, inflammation in the Gasserian ganglion of the same side, and was able to demonstrate the local presence of many gram-positive cocci. In Sattler's case (40) and in Boeck's case (39) inflammatory changes were found in the Gasserian ganglion, and in Fischl's case (19) leukæmic infiltration of the ganglion was present. In Herpes zoster of spinal distribution analogous changes in the spinal ganglia are recorded (38, 41, 42, 43).

References to the Literature and Notes.

(1) H. Tenneson.—*Traité clinique de dermatologie*, Paris, 1893, p. 116.

(2) Colombini on Herpes zoster generalisatus (1893); quoted by Fischl (19), Fasal (10), and Beyer (9). F. Mracek's *Handbuch der Hautkrankheiten* (Vienna, 1902, vol. i, p. 692), in the article on Herpes by Blaschko, contains an illustration of Colombini's case.

(3) Jean Molinié.—"Des vésicules aberrantes dans le zona," *Thèse de Paris*, 1895-6, No. 97.

(4) Haslund.—On Herpes zoster, with generalised eruption; quoted by Fischl (19), Fasal (10), and Beyer (9), from the 8th volume of the *Nordiskt Med. Arkiv*, 1897.

(5) E. Jeanselme and Leredde.—"Sur les vésicules aberrantes du zona," *Bull. et Mém. Soc. Méd. des hôpitaux de Paris*, 1898, 3 sér., vol. xv, p. 619.

(6) W. L. Ffrench.—"Herpes Zoster with Aberrant Vesicles," *Brit. Med. Journ.*, 1899, vol. i, p. 388. Man, over sixty years of age, suffered from febrile malaise, intercostal Herpes zoster, and varicella-like vesicles scattered over various parts of the body.

(7) J. A. Arkwright.—"Two cases of Herpes Zoster with a generally distributed Eruption." *St. Barth. Hosp. Journ.*, London, 1900, vol. vii, p. 172.

(8) Blaschko.—Article on "Herpes," in Franz Mracek's *Handbuch der Hautkrankheiten*, Vienna, 1902, vol. i, pp. 677–722. Copious Bibliography.

(9) R. Beyer.—"Herpes zoster mit generalisierter Lokalisation," *Arch. f. Derm. u. Syph.*, Vienna, 1906, vol. lxxviii, p. 233; *cf.* the same writer's *Inaug. Dissert.*, Griefswald, 1906.

(10) Hugo Fasal.—"Herpes zoster generalisatus," *Arch. f. Derm. u. Syph.*, Vienna, 1909, vol. xcv, p. 27.

(11) J. F. Schamberg.—"Generalised Herpes," *Journ. Amer. Med. Assoc.*, 1910, vol. liv, p. 532.

(12) G. Nobl (of Vienna).—"Zur Kenntnis des Herpes zoster generalisatus," *Wiener klin. Wochenschrift*, 1911, Jahrgang xxiv, p. 14.

(13) Friedrich Steuer.—"Ein seltener Fall von Herpes zoster gangrænosus generalisatus," *Wiener med. Wochenschr.*, 1911, lxi, column 1167. A woman, aged 76 years.

(14) Minet and Leclercq.—"Du zona avec éruption généralisée," *La Clinique*, Paris, 1911, Année vi, p. 101. Twenty-five cases collected. Reference also to work of Gaucher and Girard.

(15) F. J. Coleman, "Shingles and Chickenpox," *Guy's Hospital Gazette*, London, 1913, vol. xxvii, p. 184. A man, over seventy years of age, developed an eruption of Herpes zoster, and, about two days later, an eruption resembling typical varicella.

(16) E. Jeanselme and A. Touraine, "Zona suivi d'un éruption généralisée des vésicules aberrantes," Soc. Franç. de derm. et de syph., Paris, Meeting of July 2nd, 1914.

(17) A. Tryb (of Prague).—"Herpes zoster generalisatus," *Dermat. Wochenschrift*, Leipzig, 1914, vol. lix. p. 983. Man, aged 60 years.

(18) G. Pernet.—"Generalised Herpes Zoster," *Brit. Journ. Derm.*, London, 1914, vol. xxvi. p. 399.

(19) F. Fischl.—"Herpes zoster generalisatus bei Lucæmia lymphatica." *Arch. f. Derm. u. Syph.*, Vienna, 1913, vol. cxviii, p. 553. No mention is made in regard to whether arsenic was being used in the treatment at the time when the Herpes zoster broke out. Leukæmic infiltration of the Gasserian ganglion was found at the post-mortem examination. Many references to the literature of Herpes zoster generalisatus are given.

(20) ——— In this connection it is perhaps worth alluding to the occurrence of a generalised bullous eruption on giving antipyrin to a patient with Herpes zoster. See Frank Deas, "Bullous eruption due to Antipyrin, occurring in a patient suffering from Herpes zoster," *Brit. Journ. Derm.*, London, 1899, vol. xi, p. 194. A man, aged 34 years. The generalised eruption reached its height about five hours after taking the first dose of the medicine [which was given for pain]. Disappearance of the eruption was rapid.

(21) Johann von Bokay.—"Ueber den ätiologischen Zusammenhang der Varizellen mit gewissen Fällen von Herpes Zoster," *Wiener klin. Wochenschr.*, 1909, vol. xxii, p. 1323; also *Compte-rendu du XVI^e Congrès international de médecine*, Budapest (1909), Section X (Pédiatrie), p. 480

(22) Paul Heim.—"Herpes zoster und Varicellen," *Berliner klin. Wochenschr.*, 1912, vol. xlix, p. 2349.

(23) W. P. le Feuvre.—"Herpes zoster and Varicella," *Medical Journal of South Africa*, Johannesburg, 1914, vol. ix, p. 177. Amongst the twenty-one instances given by the author of Herpes zoster in one patient apparently giving rise to attacks of varicella in others are two observations by himself in South Africa, and many observations recorded in the *Brit. Med. Journ.* and the *Guy's Hospital Gazette*. The author likewise quotes four examples of cases of varicella being followed by Herpes zoster, and refers to various instances of a varicella-like eruption and true Herpes zoster occurring in the same patient more or less simultaneously with each other.

(24) Aikman (of Guernsey), quoted by Le Feuvre, *Medical Journal of South Africa*, Johannesburg, 1914, vol. ix, p. 178, Observation 22. A child returned to school with the remains of a varicella eruption on it. Seven days later the schoolmistress, aged 30 years, developed right thoracic Herpes zoster. She had never had varicella. Eleven days later her sister, aged 25 years, and two children attending the school, developed varicella.

(25) (*Anonymous*).—"Shingles and Chicken-pox," *Guy's Hospital Gazette*, London, 1913, vol. xxvii, p. 219. A boy, aged 13 years, developed Herpes zoster two and a half weeks after exposure to varicella infection.

(26) E. A. Dando.—"Herpes and Varicella," *Brit. Med. Journ.*, London, 1913, vol. ii, p. 1340. A patient developed Herpes zoster four weeks after the patient's son was suffering from varicella. A lady developed Herpes zoster five weeks after her daughter was suffering from varicella.

(27) J. Hepworth.—"Herpes and Varicella," *Brit. Med. Journ.*, 1914, vol. ii, p. 629. On August 24th a mother had Herpes zoster, and on September 9th her son developed a varicella eruption.

(28) John Orr.—"Herpes and Varicella," *Brit. Med. Journ.*, 1913, vol. ii, p. 1048.

(1) A man, aged 50 years, developed severe herpes of the scalp. His daughter developed varicella two weeks later.

(2) A man, aged 45 years, developed typical thoracic Herpes zoster, and three days later a varicella-like eruption.

(29) Howard Distin.—"Herpes and Varicella," *Brit. Med. Journ.*, 1915, vol. i, p. 633.

(30) M. Kaposi.—"Bemerkungen über die jüngste Zoster-Epidemie," *Verhandl. d. deut. dermat. Gesellsch.*, Vienna, 1889, vol. i, p. 57. Kaposi observed forty cases of Herpes zoster during twelve months, 1888–1889.

(31) Henry Taylor.—"An Epidemic of Herpes Zoster," *Brit. Med. Journ.*, London, 1889, vol. ii, p. 13. Taylor saw four cases of Herpes zoster in one week at Guildford, and a firm of practitioners in the same town saw nine or ten cases in the course of two months about that time.

(32) Emil Weis.—"Ueber epidemischen Zoster," *Arch. f. Derm. u. Syph.*, Vienna, 1890, vol. xxii, pp. 609–629. On p. 622 the author says that several cases of Erythema multiforme were observed during the period of the epidemic of Herpes zoster.

(33) Breuer.—"Das epidemische Auftreten der verschiedenen Herpesformen," *Inaug. Dissertation*, Breslau, 1891. Quoted by F. Fischl (reference 19).

(34) Solon Veras.—"Herpes Zoster by Contagion," *Brit. Journ. of Children's Diseases*, London, 1912, vol. ix, p. 360. Refers also to previous literature of the subject.

(35) J. Galippe.—"Un cas de zona cervical," *Bull. Soc. de Pédiatrie de Paris*, 1913, vol. xv, p. 200. Herpes zoster in two boys, living in the same house, with an interval of four or five days.

(36) F. Parkes Weber.—"The Occurrence of Acute Pneumonia during Treatment with Arsenic," *Brit. Med. Journ.*, 1913, vol. i, p. 337 (case No. ii).

(37) H. Head and A. W. Campbell.—"The Pathology of Herpes Zoster and its bearing on Sensory Localisation," *Brain*, London, 1900, vol. xxiii, p. 353.

Case 18 (p. 501). A man, aged 31 years. Herpes zoster of the right side of the face (infra-maxillary division of the fifth cranial nerve). Death from general paralysis thirty days after the eruption. Post-mortem, the right Gasserian ganglion showed in its corresponding portion a focal destructive lesion.

Case 19 (p. 509). A man, aged 43 years. Right frontal Herpes zoster (ophthalmic division of the fifth cranial nerve). Death from general paralysis 190 days after the eruption. Post-mortem, there was a focus of disease in the part of the right Gasserian ganglion corresponding to the first division of the fifth nerve. The authors refer likewise to previous literature on the subject.

(38) F. G. F. von Bärensprung.—"Die Gürtelkrankheit," *Annalen des Charité-Krankenhauses zu Berlin*, 1861, ix, part 2, p. 40; 1862, x, part 1, p. 37; 1863, xi, part 2, p. 96. It is in the third part (1863) of von Bärensprung's elaborate series of articles on Herpes zoster that he describes a case of thoracic Herpes zoster in a boy, aged 1½ years, who died of tuberculosis six weeks after the commencement of the eruption. The necropsy showed inflammation of the corresponding spinal ganglia of the affected side.

(39) C. Boeck, of Christiania (quoted by A. Sunde, reference 45), in 1878, found purulent inflammation of the Gasserian ganglion in a case of facial Herpes zoster.

(40) H. Sattler.—("Verein deut. Aerzte in Prag," January 25th, 1889), *Wiener med. Wochenschr.*, 1889, vol. xxxix, column 328. Herpes zoster ophthalmicus in a man, aged 85 years, after carbon-monoxide poisoning. Death occurred fourteen days after the eruption. Severe inflammatory changes were found in the Gasserian ganglion of the affected side.

(41) V. Magnus.—*Norsk Mag. for Laegevid.*, 1902, p. 517; 1903, p. 877; 1906, p. 1429; quoted by A. Sunde (reference 45). A case of Herpes zoster with motor symptoms. Necropsy three weeks after the herpes eruption. He found Gram-positive diplococci in the anterior horns of gray matter, but none in the affected spinal ganglia, which only showed ordinary inflammatory changes.

(42) O. Scheel (1904), quoted by A. Sunde (reference 45). Inflammation of spinal ganglia in cases of Herpes zoster (death some weeks after the Herpes zoster).

(43) A. de Besche (1910), quoted by A. Sunde (reference 45). Inflammation of spinal ganglia in cases of Herpes zoster (death some weeks after the Herpes zoster).

(44) André-Thomas and Henyer.—"Anatomie pathologique d'un cas de zona ophtalmique," Société de Neurologie, Paris, Meeting of February 29th, 1912. (*Revue Neurologique*, Paris, 1912, vol. xxiii, p. 381.) The authors found changes in the Gasserian ganglion, confirming the theory of Head and Campbell.

(45) Anton Sunde (of Christiania).—"Herpes zoster frontalis mit Bakterienbefund im Ganglion Gasseri," *Deut. med. Wochenschr.*, 1913, Jahrgang xxxix, p. 849.

(46) ——— In this connection it is interesting to note that Herpes zoster seems to be of rare occurrence in cases of Tabes dorsalis and syringomyelia. *Cf.* A. Westphal, "Ein Fall von Tabes dorsalis mit Herpes zoster," *Charité-Annalen*, Berlin, 1897, Jahrgang xxii, p. 655. Westphal refers to reports by von Leyden, Erb, and Charcot, regarding the occurrence of Herpes zoster in patients with Tabes dorsalis.

(47) F. E. Batten.—Article on "Polio-encephalo-myelitis," in Garrod, Batten, and Thursfield's *Diseases of Children*, London, 1913, p. 767.

(48) ——— In this connection it should be noted that Herpes zoster may appear in, and is one of the more common cutaneous manifestations of, epidemic cerebro-spinal meningitis. In tuberculous meningitis it does also, but very rarely, occur. See W. Evans, "Meningitic Herpes," *Brit. Journ. Derm.*, London, 1900, vol. xii, p. 83. See also P. Durand, regarding the presence of the meningococcus in the herpetic vesicles in cerebro-spinal meningitis—communication to a medical society of Lyons, *Presse Médicale*, Paris, January 3rd, 1914, p. 11.

(49) L. Nielsen.—"Ueber das Auftreten von Herpes zoster während Arsenikbehandlung," *Monatsheft für prakt. Dermatologie*, Hamburg, 1890, vol. xi, p. 302.

(50) Berthold Stein.—"Ueber den Herpes zoster arsenicalis," *Inaug. Dissert.* Heidelberg, 1901.

(51) Adolf Schmidt.—"Herpetische Eruptionen als Vorstadium eines Hautcarcinoms neben Herpes zoster," *Arch. f. Derm. u. Syph.*, Vienna, 1904, vol. lxx, p. 321. The case was perhaps one of Herpes zoster occurring in a patient under arsenical treatment.

(52) T. E. Leudet.—*Études de Pathologie et de Clinique Médicales*, Paris, 1891, vol. ii, p. 564: "Le zona peut-être l'effet d'une intoxication, comme celle par l'oxyde de carbone." *Cf.* Leudet's original paper: "Recherches sur les troubles des nerfs périphériques . . . consécutifs à l'asphyxie par la vapeur de charbon." *Arch. Gén. de méd.*, Paris, 1865, vi^{e} Sér., vol. v, p. 513. Ivor J. Davies, in his account of the "Carbon Monoxide Poisoning in the Senghenydd Explosion" (*Brit. Med. Journ.*, 1914, vol. ii, p. 57), mentions cutaneous erythematous lesions as occurring in nine of the cases. In one case œdema, vesicles and bullæ were associated with the erythema (*cf.* also reference 39 in the present paper).

(53) F. Parkes Weber.—"Herpes Zoster with Paralysis of Arm," *Brit. Journ. Derm.*, London, 1915, vol. xxvii, p. 408. This paper gives references to many records of Herpes zoster associated with paralyses and, in some instances, muscular wasting, as well as to many cases associated with unusual sensory disturbances, especially of the special senses of hearing, smelling and tasting. In the cases associated with paralysis, the paralysed parts generally correspond fairly well to the distribution of the Herpes zoster, but in exceptional instances the paralysis is located at a distance from the site of the herpetic eruption. Thus Mr. G. J. Jenkins kindly tells me of a recent case (a middle-aged man) seen by him, in which thoracic Herpes zoster (lower thorax) was associated with paralysis of the vocal cord on the opposite side; gradual recovery took place, though slight paresis of the vocal cord still manifests itself occasionally.

(54) Arthur Jaehne.—"Zur klinik des Herpes zoster oticus," *Archiv für Ohrenheilkunde*, Leipzig, 1914, vol. xciii, p. 178. The patient was a young man, aged 21 years, who fell ill with fever, lassitude, and jaundice. A few days later an eruption of Herpes zoster of the pinna and external auditory meatus of the right side showed itself. Three days later facial paralysis occurred and was accompanied by severe auditory disturbance, and followed by deafness. There was likewise loss of taste in the right half of the tongue. The facial paralysis was noted to be rather less after half a year, but the auditory and gustatory symptoms persisted. Jaehne gives numerous references to the literature of Herpes zoster oticus.

(55) H. Wilbrand and A. Saenger.—*Die Neurologie des Auges*, Wiesbaden, 1901, vol. ii. See pp. 188–206 for discussion on the nature and ætiology of Herpes zoster, with abundant references to literature of the subject. See pp. 176–183, in regard to the complications, especially the paralytic nervous complications, of Herpes zoster ophthalmicus.

(56) J. R. Hunt.—"The Paralytic Complications of Herpes zoster of the Cephalic Extremity," *Journ. Amer. Med. Assoc.*, 1909, vol. liii, p. 1456. References to many of Hunt's other writings on the subject are given in F. P. Weber's article in the *Brit. Journ. Derm.*, 1915, vol. xxvii, p. 408 (reference 53).

(57) Norman Sharpe.—"Herpes Zoster of the Cephalic Extremity," *Amer. Journ. Med. Sci.*, Philadelphia, 1915, vol. cxlix, p. 725.

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SPECIFIC HYPERSENSITIVENESS OR ALLERGY IN RELATION TO CERTAIN ERUPTIONS OF MICROBIC ORIGIN.

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Dr. Sequeira (1), in his useful commentary on Rist and Rolland's "Studies of Tuberculous Re-infection" (2), remarks very truly that the new conception of tuberculides suggested by these studies demands the close attention of Dermatologists. The view that the tuberculides are virtually "phenomena of Koch" induced by auto-inoculation by virile tubercle bacilli in a subject hypersensitised by previous infection is one of great interest. It calls, too, for consideration because the same idea may be adapted to the secondary eruptions of syphilis and, possibly, to certain other skin affections of microbic origin.

A striking feature of the "tuberculides," in contrast with other tuberculous affections of the skin, is that they show no tendency to local spread (as do the lesions of Lupus vulgaris, for example), and that they arrive eventually at a spontaneous cure.

The fact that most observers have failed to demonstrate the presence of living tubercle bacilli in the tuberculides has been looked upon as an explanation of their transitory nature, and has led to the theory that they are due to tuberculo-toxins, or perhaps to dead or attenuated bacilli, which have not the power to multiply locally and thus to cause persistent or spreading lesions.

In support of this theory it has been many times demonstrated that tuberculides may be experimentally or accidentally imitated, or, as some claim, exactly reproduced in tuberculous persons by intradermic injections of tuberculin or of bacillary emulsion; and Dr. Sequeira recalls several examples of "Erythema induratum" and of "Lichen scrofulosorum" following such injections in tuberculous subjects.

An important point, which is no doubt generally recognised, but which is not always clearly brought out, is that these eruptions can occur only in persons who have been previously infected by the tubercle bacillus, and whose system is consequently hypersensitive, or, as we now say, has altered conditions of reaction—is in a state of allergy towards tubercle bacilli or their toxins. Tuberculides are in fact, according to this view, to be regarded as tuberculin "cuti-reactions" in persons hypersensitised by tuberculosis.

But according to the hypothesis of Rist and Rolland — a hypothesis which has indeed already been put forward by Jadassohn (3) and his pupil—we need not suppose that the exciting agent of tuberculides must necessarily be tuberculo-toxins or dead or attenuated bacilli. They may very well be (and according to these observers, in all probability they are) living virulent bacilli, which are carried to the skin in a specifically allergic subject by the blood-stream, and there excite so prompt and violent a reaction that the bacilli have no time to multiply, but are immediately destroyed. In other words, each "tuberculide" is, strictly speaking, an example of the "phenomenon of Koch" rather than a "cuti-reaction of von Pirquet." Rist and Rolland have virtually repeated and confirmed the often-quoted original experiment of Koch (4) which demonstrated that (in Koch's words) "the injected tubercle bacilli act quite differently upon the skin of a healthy as compared with that of a tuberculous guinea-pig." But to-day we lay stress upon the altered conditions of reaction of the infected subject, rather than upon the changed action of the bacillus.

Rist and Rolland's experiments cannot be taken as an actual proof of the origin of tuberculides from virulent tubercle bacilli, but only of the probability; for we know that there is no real distinction between the effect of an intracutaneous inoculation with living tubercle bacilli and of that of an intradermic tuberculin injection, provided the subject be allergic to tubercle. Koch himself noted that "this striking change does not belong exclusively to living tubercle bacilli, but occurs just the same with dead tubercle bacilli, whether they have been killed by prolonged low temperature, or by heat, or by certain chemicals." The indolent character of many of the tuberculides as compared with artificially produced tuberculin reactions has been explained by Jadassohn by the supposition that the endotoxins, which are only slowly absorbed from acid-fast bacilli, continue to take effect after the bacilli are killed.

These facts and the deductions from them have been already clearly put by Dr. Sequeira in his review of Rist and Rolland's monograph, but their interest and importance will excuse their repetition here. There is, however, another aspect of the subject which must be considered—namely, that if we accept the view that tuberculides are due to living, virulent bacilli, it is necessary to explain why in some tuberculous subjects a shower of virile bacilli give rise to tuberculides, while in another case they produce real lupus nodules, which may eventually increase by local extension.

We see the former event in the case of acute miliary lupus supervening upon a more chronic tuberculous infection, and, more familiarly, in cases of multiple lupus after measles in a tuberculous subject. Such patients, being already subjects of tuberculosis, ought, one might argue, to be protected against re-infection by auto-inoculation, so that tuberculides, and not true lupus nodules, should result from bacilli brought to the skin by the blood-stream. An explanation is to be found in the fact that in some cases of tuberculosis the allergic condition is very low, as is shown by these cases giving only feeble cuti-reactions to tuberculin, and they are thus unable to resist the re-infection. It is interesting to note in this connection that von Pirquet has demonstrated that in tuberculous subjects with measles or with scarlet fever the cuti-reaction to tuberculin is altogether in abeyance during the height of the disease, though it returns during convalescence. On the other hand, patients with tuberculides are always found to give a marked cuti-reaction, which indicates a high allergic condition, and protection against auto-reinfection.

If we turn now to the consideration of syphilis, it is interesting to find that the eruptions of the different stages can be explained by our knowledge of these immunity reactions. The chancre represents the local result of the initial infection. By this infection the subject becomes hypersensitised or allergic towards the micro-organisms of syphilis, and thus protected from a second infection. The secondary eruptions may be looked upon as "cuti-reactions" or as "phenomena of Koch," a result of the arrival of spirochetes in the skin of the now highly allergic subject. This explains why these eruptions are generalised, and why they eventually pass away by spontaneous cure. The patient now remains allergic and protected for a varying period: but eventually the allergic condition abates and reinfections by auto-inoculation may take place which show a tendency to persist and to spread. These are the tertiary eruptions.

Thus, the secondary syphilides are analogous to the tuberculides.

The later syphilides are analogous to lupus by auto-inoculation. These views in regard to the eruptions of syphilis were advanced by the writer (5) in 1912, but they are by no means new, for so long ago as 1907 Jadassohn (6) conceived the idea of roseola and early syphilides as cuti-reactions in a specifically hypersensitised subject. In a note in the bibliography of an article on syphilis in Neisser's *Festschrift*, he has the following paragraph: "If the experiments of Von Pirquet on re-vaccination and his interpretation of them be confirmed, then one may establish the following conception: The primary period (of syphilis), as a result of the first inoculation, is able to protect the body against re-infection, apparently through antibody substances. During this first period (*i. e.* at the commencement of 'secondary syphilis') the skin becomes impregnated with protective bodies, and it follows that the importation of spirochetes by the blood-stream leads to a reaction (roseola) which overcomes the spirochete. Later these protective substances are no longer in evidence; but they quickly become formed, as in normal individuals, and thus are produced the somewhat later efflorescences. The roseola is a reaction without incubation period, the papule arises after a short inoculation."

Again, in 1912, Tièche (7), a pupil of Jadassohn, wrote on the same subject. He regarded the roseola as an anaphylactic reaction towards the presence of spirochetes, few in number, which had been demonstrated in these lesions. The reaction is rapid, and the spirochetes in these lesions immediately perish; the later secondary syphilides are of longer duration, because the anaphylaxis is diminished and the spirochetes are not killed at once.

But the tuberculides and the secondary syphilides are not the only eruptions whose characters of symmetrical generalised distribution and of advance towards spontaneous cure may be accounted for upon the hypothesis of Koch phenomena in allergic subjects. It is possible also to explain in this manner the eruption of measles, of enteric fever (in the roseola of which the typhoid bacillus has been demonstrated), of varicella, and of smallpox. The infection by the micro-organisms of these diseases produces a condition of allergy, and the eruptions are cuti-reactions or phenomena of Koch due to auto-inoculation of the skin at the height of the allergic condition.

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FOUR CASES OF SCLERODERMIA ASSOCIATED WITH DISEASE OF THE THYROID GLAND.

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I PURPOSE in this communication to describe four cases of sclerodermia associated with disease of the thyroid gland.

One patient (Case 4) has suffered from myxœdema for seventeen years, and the sclerodermia developed while the symptoms of myxœdema have been entirely controlled by thyroid treatment. This observation I believe to be unique. In the other three cases the sclerodermia is associated with Graves' disease.

I have notes of 22 cases of sclerodermia seen during recent years in private practice and at the London Hospital, 18 of which were females and 4 males. Besides those now put on record there was 1 case of pure guttate type, reported by Silva Jones (1), 1 of band form on the thigh and leg with guttate lesions on the trunk (2), 15 of morphœaic sclerodermia, and 1 of the diffuse type. Of the 22 cases, 4 were associated with affections of the thyroid gland.

CASE 1: *Sclerodermia of legs associated with Graves' disease.*—Mary S—, single, consulted me at the London Hospital on December 20th, 1909. She was then aged 22 years, and had passed all her life in Essex. She attended the hospital on account of an ulcer on the left leg. The ulcer had been in existence for several months and had failed to respond to the usual methods of treatment. When I first saw her it was evident that the ulcer was a secondary phenomenon. The lower half of the left leg was in a condition of sclerodermia and the ulcer had resulted from a slight injury. The sclerodermia extended the whole way round the lower half of the left leg. Its upper margin was fairly well defined, but there was no lilac colour such as is usually present in morphœa. The sclerosed skin was pale, tough, and could not be pinched up. There were no telangiectases and no pigmentation. Over the middle of the area on the shin there was an ulcer the size of a two-shilling piece with a shelving edge and a base covered with flabby granulations. There was also an area of sclerodermia about the size of the palm over the middle of the inner side of the right leg.

General condition.—On examination the patient was a thoroughly well-developed young woman, the skin was pale, and the mucous membrane of the lips and gums showed there was distinct anæmia.

The eyes were slightly prominent and von Graefe's sign was present.

The tongue was protruded without tremor.

The thyroid gland was enlarged and prominent. The carotid arteries showed visible pulsation in the neck. Tachycardia was present on every occasion the patient was examined, the pulse-rate varying from 112 to 120 per minute. The heart-sounds were normal and the apex was not displaced.

Fine tremor was well marked in the hand. There was no evidence of visceral disease, and the Wassermann reaction was negative.

Progress.—The patient attended the hospital at rather irregular intervals until this year. The ulcer proved exceedingly difficult to heal, and many different applications were used, both of a stimulating and antiseptic character. Stimulant doses of X-rays were also given. The ulcer has at last healed after prolonged rest, but it is quite possible that it may break down again.

General treatment.—As benefit has been reported by the thyroid treatment in cases of sclerodermia, I gave the patient two courses of thyroid extract, but without benefit to the ulcer or to the skin condition. The general condition appeared to be made worse, the tachycardia and tremor increasing.

From July, 1914, to the end of that year, the swollen thyroid gland was treated by X-rays through an aluminium screen, and this treatment had a definite effect upon the general symptoms and may have contributed to the healing of the ulcer, but it had no appreciable effect upon the sclerodermia.

Case 2. *Sclerodermia of trunk with Graves' disease.**—G. F—, aged 22 years, single, came to the London Hospital on December 21st, 1915, on the recommendation of Dr. Smulian. She had suffered from measles and scarlet fever in childhood, she had never had rheumatism. For some years she has had a swelling in the neck, and two months ago she noticed some white patches on the front of the chest. The thyroid gland is very large, the eyeballs are prominent, there is a fine tremor of the hand and tongue, there is no excessive sweating, but the patient complains of flushing. The pulse rate had been as high as 128. She states that she has been very irritable of late, micturition is somewhat frequent, and there is some increase in the quantity of the urine passed. The patient sleeps well, the bowels are opened regularly without medicine.

Sclerodermia.—There is a large oval patch extending obliquely across the left clavicle. Its surface is of ivory whiteness and remarkably smooth. It is surrounded by a lilac margin about a finger's breadth in width. Extending from it towards the middle line are numerous small spots of the same character. There is another area of smaller dimensions over the right side in the middle of the sternum, and numerous macular areas below it. On the back there are two oval patches, one situated at the level of the spine on the left scapula is about the size of a five-shilling piece, and there is a somewhat larger patch at a slightly lower level along the base of the right scapula. There are a few macular areas on each hip, just above the trochanters. The *tâche* is obtained very easily, and the patient is anæmic and obviously of a nervous temperament. She suffers frequently from headaches, and the pupils are dilated. The Wassermann reaction is negative. The skin of the arms shows common Keratosis follicularis.

Case 3. *Symmetrical Sclerodermia associated with Graves' disease.* Mrs. X—, aged 59 years. Symmetrical pear-shaped patches of sclerodermia on each leg, the apex of each being upwards and at the head of the fibula. On the right thigh, about the middle of the posterior surface, was a small patch also oval in shape, but not more than three-quarters of an inch in length. The lilac edge of the white patches was well marked. There were tachycardia, some proptosis and prominence of the thyroid gland. A history of heat and flushings was also given and the *tâche* was well marked.

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* Shown at the Royal Society of Medicine (Dermatological Section), January 20th, 1916 (see p. 69).

This patient was only seen once. The Wassermann reaction was not examined. There was no history or evidence of syphilis. The patient was a wasted, nervous woman.

CASE 4. *Sclerodermia of both legs developing in a myxœdematous patient taking thyroid.**—Alice M—, a married woman, came under my care at the London Hospital on October 29th, 1900. She was then aged 42 years. She had had six children, who were in good health, and one miscarriage. She had been in failing health for nearly two years before I saw her, and had been admitted into a provincial cottage hospital as possibly suffering from cancer of the liver. She came to the Skin-Department of the London Hospital on account of a dry eczematous condition of the hands. It was immediately obvious that she was suffering from myxœdema. The skin was dry, the hair had been falling out freely and was then very thin, there was a pink flush on each cheek, and the rest of the skin had a characteristic waxen appearance. The lips were thickened, and the patient complained of feeling cold. She was rather deaf, and her speech was slow. She stated that she had not perspired for a long time. On examination the thyroid gland could not be felt, the fingers, on palpating, coming directly down on the trachea.

Progress.—This patient has attended my department for the past fifteen years, and throughout has taken thyroid extract. At first I began with a very small dose, and increased it until the patient complained of flushing, palpitation, etc., *i. e.* until I had demonstrated the reaction to thyroid. I then diminished the dose until I could keep the symptoms entirely in control, and for years the patient has taken 1 gr. of the thyroid extract three times a day. In passing it is interesting to note that the patient shows a remarkable sensitiveness to the drug. During the long period she has been under my care she has twice complained of the tablets doing her no good, and on inquiry each time I have found that a temporary change has taken place in the source of supply of the drug.

The patient has enjoyed good health and her skin gave no trouble until about a year ago. She has complained from time to time of "rheumatic pains," in the lower extremities chiefly.

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* Shown at Royal Society of Medicine (Dermatological Section), December 16th, 1915 (see p. 46).

Present condition.—The patient is now aged 56 years. She shows no sign of myxœdema. She is rather fresh-coloured, brisk in her movements, and her speech is not affected. There is no evidence of pulmonary, cardiac or hepatic disease. The bowels act only with the use of saline aperients. The urine is of normal character.

The Wassermann reaction is negative.

Sclerodermia.—For a great part of the past year the patient has noticed that the skin on the lower half of both legs has been very hard, and she has had "rheumatic" pains in these parts. An area of sclerodermia extends from below the middle of each leg to just above the instep. The skin is rather more yellow than the rest of the integument, it is very tough, feels like hide, and cannot be pinched up. There are no telangiectases, but below the sclerosed areas there is on each side of both feet a very large plexus of dilated veins, which I presume to be due to pressure of the sclerodermia on the venous trunks of the leg. The area affected on the right leg is more extensive than that on the left, but in either it forms a band which envelops the limb.

The obvious interest of this case is the development of sclerodermia in a patient suffering from myxœdema, which disease has been controlled for many years by thyroid extract.

The *pathogenesis of sclerodermia* is still obscure, and the most cursory survey of the literature shows that this cutaneous affection occurs in connection with such a variety of conditions that it is difficult to believe that many of the casual relationships which have been suggested can be accepted. Heller (3) advanced the hypothesis that sclerodermia is due to a general or local lymphatic obstruction, and in support of this contention a case associated with obstruction of the thoracic duct was reported. Hoppe-Seyler (4), impressed with the occurrence of the disease in two children from the same place, suspected an infectious origin. No micro-organisms have been demonstrated in the cases examined, but it is worthy of note that the disease has been seen as a sequel to scarlatina (Pringle), diphtheria (Marsh), erysipelas (Chauffard), infectious tonsillitis, pneumonia, tuberculosis, influenza, malaria, measles, etc. Many references are given by Luithlen in this connection, and their number justifies the suggestion of Dana (5) that any infectious disease may be followed by sclerodermia. The most generally accepted is that it is a tropho- or angiotropho-neurosis, caused by changes in the nervous system (Lewin and Heller (6)). The peculiar distribution seen in some cases of morphœic sclerodermia supports this contention. It is more difficult to accept this hypothesis in cases of diffuse sclerodermia, which may possibly have a different cause. Jacquet (7) has described changes in the spinal cord, "myélite cavitaire," in sclerodermia, but Mott (8) failed to find any evidence of disease. J. L. Steven (9) found atrophy of the grey matter of the anterior horn of the cord on the same side as an area of localised sclerodermia.

Degeneration of the peripheral nerves and of the cord has been described by various authors (*vide* Luithlen (10)), but there appear to be no recent observations. Brissaud (11) maintained that the skin affection depended upon disease of the sympathetic, and its occasional association with anomalies of pigmentation may be held to be in support of the hypothesis, but there is no conclusive evidence.

Another hypothesis is that sclerodermia is the result of extensive endarteritis. In this connection it is interesting to note its occasional co-existence with Raynaud's disease. Cases are recorded by Hutchinson (12). Favier (12) collected fourteen cases with this association.

This naturally opens up the question of the possibility of there being a syphilitic basis in some cases of sclerodermia, as some cases of Raynaud's disease have been shown to have a positive Wassermann reaction. In Luithlen's article in Mracek's Handbuch (10) there are numerous references to the treatment of sclerodermia by anti-syphilitic remedies during the latter half of the nineteenth century (Rilliet, Arning, Cohn, etc.), and one (Curzio) in the eighteenth century. Lustgarten (13) first recorded a positive Wassermann reaction in a case of sclerodermia, and Whitehouse (14) had the blood examined in seven cases. In five of the diffuse type three gave a strongly positive reaction, one faintly positive, and one negative. Jeanselme and Tourraine (15) describe the case of a woman, aged 48 years, with sclerodermia of the face, trunk, and extremities, whose blood gave a positive Wassermann reaction and who improved remarkably under anti-syphilitic treatment. In this case there was marked cerebro-spinal lymphocytosis. Brocq, Fernet, and Maurel (16) also reported a case of diffuse and rapidly-spreading sclerodermia in the course of secondary syphilis. The patient was a male, aged 32 years; his blood gave a positive Wassermann reaction, but the cerebro-spinal fluid was negative to the last.

In Osler's Case V (17), in which there was sclerodermia associated with Graves' disease, the patient had had syphilis ten years before, but had been treated for five years.

Three patients described in this communication had a negative Wassermann reaction.

SCLERODERMIA ASSOCIATED WITH AFFECTIONS OF THE THYROID GLAND.

Luithlen (10) states that Eulenberg was the first to record the co-existence of sclerodermia and Graves' disease. The thesis of Samouilson (18), "De la co-éxistence de la sclérodermie et des altérations du corps thyroide," deals with the literature to 1898. Roques (19) in an article on "Opotherapy in Sclerodermia" states that of 31 cases in which the state of the thyroid gland was mentioned there were clinical signs of the organ being affected in 22. In 14 cases the thyroid was described as being small or imperceptible. In 8 cases it was hypertrophied. In 9 cases it was reported as being normal. It seems probable that local conditions may have some influence on the frequency of the co-existence of these conditions, for Dittisheim (20) found 8 cases of sclerodermia in 17 cases of exophthalmic goitre, *i. e.* in 47 per cent. Osler's Case V (17) was a male patient, aged 40 years, with an advanced stage of Graves' disease with remarkable sclerodermia of both legs. The patient had had a severe attack of syphilis ten years before. The same author's Case VII, a male, aged 49 years, suffering from sclerodermia of the hands, fingers, and cheeks, suffered from tachycardia, but there was no evidence of thyroid hypertrophy.

Thyroid atrophy, according to Roques' collection of cases, appears more common than hypertrophy. In Singer's case (21) one lobe of the thyroid was much reduced and fibrous; in Hektoen's case (22) the gland was atrophic and only weighed 14 grm. In Uhlenhuth's case (23) the organ had completely disappeared. Bouchet and Dujol (24) also describe a recent case associated with thyroid atrophy.

The co-existence of serious disease of the thyroid gland with sclerodermia naturally suggested treatment of the cutaneous condition by thyroid extract. Roques (*loc. cit.*) collected 67 cases in which this form of opotherapy had been practised. The results were as follows :

Cures	4	5·97 per cent.
Improvement	32	47 ,,
No effect	31	46 ,,

I have used thyroid extract in the treatment of a number of cases, and I agree with Osler's statement that "thyroid extract has no specific action in sclerodermia as it has in myxœdema. In no case did the skin of the affected regions become softened or regain its normal consistence." Other observers quoted by Roques have been more fortunate, and perhaps the most remarkable case of all is one reported in 1912 by Nicolas and Moutot (25). The patient was a child aged 3 years, and the lesions were in plaques. Cure was *complete* in four months.

Association of Sclerodermia with Affections of the other Ductless Glands, etc.

Cases are on record in which Addison's disease has co-existed with sclerodermia. But in considering this association it is important to bear in mind Osler's caution that increase in the pigment of the skin is a very striking feature in sclerodermia. It occurred in 144 of the 508 cases collected by Lewin and Heller (6). Alquier and Touchard (26) quote cases in which Addison's disease and sclerodermia co-existed. Winfield (27) also described an interesting case in a woman aged 52 years in whom there was diffuse sclerodermia with Addison's disease and Raynaud's phenomena. Sclerodermia with acromegaly has been recorded by Alquier and Touchard (26) and by L. Wernie (28).

Renon (29), believing sclerodermia to be due to polyglandular insufficiency, recommended thyro-ovarian treatment. Dupré and Kahn (30) followed the same lines, but without benefit, in cases of sclerodermia associated with Raynaud's disease. Schwerdt (31), on the assumption that sclerodermia is the effect of an intestinal toxine which the affected mesenteric glands cannot neutralise, gave mesenteric gland (0·3 grm. a day) in certain cases.

The consideration of these observations shows that our knowledge of the cause of this interesting condition is limited. I think we may leave out of account lymphatic obstruction as a cause. It appears probable that one type, the localised band variety of morphœa, has a nerve basis, and they would be properly considered to be trophoneuroses. Have we any ground for looking upon sclerodermia as due to thyroid disease? It is true that a certain proportion of the cases are associated with affections of this gland, but there is nothing to warrant the conclusion that alterations in the activity of the gland or of its secretion are actually causative of sclerodermia. The very fact that sclerodermia has been known to occur both in thyroid atrophy and thyroid hypertrophy makes one cautious, and my fourth case, in which the sclerodermia developed in a myxœdematous patient under thyroid treatment, seems sufficient to negative the view that sclerodermia develops as a result of deficient or excessive thyroid secretion. It is impossible to exclude the effects of changes in the character of the secretion. Possibly also the sclerodermia and the thyroid changes may cover a common cause, at present unknown.

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ROYAL SOCIETY OF MEDICINE.

DERMATOLOGICAL SECTION.

Meeting held December 16th, 1915, Dr. J. H. Stowers, President of the Section, in the Chair.

Dr. E. G. Graham Little showed a case of *Granuloma annulare with a widespread follicular eruption.* The patient was a young officer in good health. For about a year he had noted the eruption on his hands and knees. This was in the form of a ridge of white nodules closely aggregated together and arranged in the ringed distribution so typical of the disease described by Radcliffe-Crocker under this name. There were several such small rings on a patch at the base of the middle and ring-fingers on the dorsum of each hand. The skin included within the ridge was of a bluish tinge, showing no atrophy or other change. On the knees the eruption was less diffuse but equally characteristic. Itching was very moderate. The case offered many dissimilarities clinically as compared with the patient brought forward by the same exhibitor at the last meeting of the Section, a little girl, who showed the variety of the disease known as Erythema elevatum diutinum. The follicular eruption in the present case, which was present on the thighs, legs, arms, and forearms, had been noted from early childhood, and might be regarded as an exaggerated Lichen pilaris, but there were some lesions not peripilar, and showing a fine necrotic centre, rather suggestive of an abortive acneiform tuberculide. The tuberculous associations of Granuloma annulare which had been recorded in a number of cases made the occurrence of a follicular eruption, which also might be tuberculous, of some special interest. There was, however, no family or personal history of tubercle in this patient.

The **President** did not see any direct connection between the lesions upon the hands and the condition of the legs of this patient. There were many persons whose skins presented the same appearance as did the legs of this officer, apart from accompanying disease.

Dr. E. G. **Graham Little** also showed a case of (?) *Lichen planus.* The patient was a Hindu medical student, aged 22 years, in his third year at Edinburgh. He was of somewhat delicate physique, and appeared to suffer from the cold. During the past twelvemonth the eruption present had appeared in the form of bluish, somewhat verrucose inflammatory patches on the forearms, back of trunk, and scalp. Over the left eyebrow there was a disk-shaped warty patch the size of a sixpence. On the dorsum of the right foot and at its outer edge there was a linear warty ridge circumscribing a deeply red inflammatory patch covering the outer surface of the foot. On the plantar surface of both feet, but much more markedly on the right, there was a granular warty condition occupying the whole sole. On the abdomen, just above Poupart's ligament, on both sides there was an area covered by flat papular lesions very much like a retroceding Lichen planus. The mucosæ showed nothing abnormal. Sections were obtained from a lesion excised from the arm. These showed a very extensive and uniform infiltration of mononuclear cells just below the rete, the interpapillary processes of which were flattened down by the pressure of the cells. The granular layer was not increased, as was so characteristic a feature of Lichen planus, and there was little or no acanthosis. There was no appearance of foci of deep-seated infiltration, and no giant cells or other indications of tuberculous causation. The disease had appeared only some years after his arrival in this country. The Wassermann reaction was negative. The exhibitor did not think that either the clinical or histological features sustained the diagnosis of tubercle, but he would make further investigations, and in particular would obtain an experimental inoculation of a guinea-pig with tissue from one of the lesions and report later.

Dr. PRINGLE ventured, with some confidence, to suggest that this was a tuberculous affection of the skin. The scars of the healed lesions, the spreading disease on the foot, and the outlying lesions on the forehead and other parts appeared to him to be deposits in the true skin presenting all the characteristics of tuberculous tissue. He did not know whether the von Pirquet test had been done, but in the absence of syphilis, which the objective characters did not suggest to him, he did not see what else the disease could be.

Dr. ADAMSON agreed with Dr. Pringle that the eruption was of tuberculous nature, and regarded it as acute multiple lupus. About two years ago he showed a similar case of multiple lupus appearing in an adult. In that case the lupus patches entirely disappeared after six months' treatment by internal administration of iodogenol, prescribed by Dr. Abadie, of Paris.

Dr. A. EDDOWES inclined to agree with the last two speakers. When he first saw the case the idea of lupus came into his mind. But Dr. Little remarking that this was somewhat similar to lichen in some respects recalled to his mind that he had at present a patient under his care who had a small patch which commenced first as Lichen spinulosus; each spine was very prominent. The patch seemed inclined to cease spreading, and the spinous processes were falling out. The condition might be described as lichenisation, without the usual excessive thickening and hardening of the horny layer. If he could induce his patient to give him a section he would exhibit it, and would try to bring the patient also.

The PRESIDENT said that a few lesions upon the feet of the patient were certainly suggestive of Lichen planus, but he was in accord with those who regarded them as tuberculous manifestations.

Dr. W. KNOWSLEY SIBLEY showed a case for *diagnosis* (? *tuberculosis*). The patient, A. A—, was a married man, aged 27 years, a labourer on the railway. His mother died at the age of 42 from consumption. He had never had any serious illness. He had been married eight years, and had four children, all healthy. His wife had not had any miscarriages. The condition of the skin came on shortly after marriage, eight years ago, the first lesion appearing on the knuckle of the left hand, which he described as a gathering full of pus, which after a time healed and left a scar. Shortly after, other similar lesions appeared on other parts of the body. He considered he had been incapacitated and on the sick list for about six months each year. On one occasion he was ill and away from work for six months. The lesions were painless when they first appeared, but they became painful after a few days and looked like superficial abscesses, all of which left distinct scars. Most of these were circular, about the size of a shilling, and looked like vaccination marks. They were not pigmented. The condition had chiefly affected the arms, forearms, palms, legs, especially about the knees, also the soles. They were slightly distributed over the shoulders, more abundant over the buttocks, all being more or less symmetrically arranged. Scars were also present on the face and head. A few minute punctate lesions were present on the dorsum of the hands. There had never been any affection of the mucous membranes. The patient had lost most of his teeth early in life from caries, otherwise he appeared to be a well-preserved, healthy man.

The *Staphylococcus albus* was isolated from one of the recent lesions. The Wassermann and von Pirquet reactions were negative. The blood count was as follows: Red cells, 4,650,000 per cubic millimetre; white cells, 4,800 per cubic millimetre. Differential leucocyte count: Polymorphonulcear leucocytes, 67·5 per cent.; lymphocytes (small), 25·5 per cent.; lymphocytes (large), 5 per cent.; eosinophiles 1 per cent.; basophiles, 1 per cent. The urine did not contain either albumin or sugar.

When he first saw the case in the out-patient department it struck him as a recurrent bullous eruption on account of the regularity of the scarring; but on investigation there was no history of bullæ. What then occurred to him was, Was it a tuberculous process? But against that was the fact that so many of the lesions got perfectly well with little or no treatment. Most of the lesions had got well, one or two had left typical scrofulous scarring, but their general circular and clean-cut character was against their being tubercular. Apparently they had never affected his health to any extent. He presumed it was not a chronic staphylococcus infection occurring over and over again. The question of its being artefacta also occurred to him; but he thought that was excluded by the perfect symmetry of the lesions, and there were very few irregular or linear ones. Sporotrichosis must also be excluded, and he had not been able to find anything of that nature. He had not yet been able to have a biopsy, but a portion from the thickening over the right knuckle might well be examined. There had never been any affection of the nails, nor of the mucous membranes.

Dr. TRAVERS SMITH suggested the diagnosis of angioneurosis. He had had one case not dissimilar to this, and the subsequent scarring was very much like what he saw in this case.

Dr. J. H. **Sequeira** asked Dr. Sibley whether there was any seasonal variation in this eruption: whether it is worse in the winter than in the summer? [Dr. **Sibley** did not think it was; he had asked him that question.] He thought it was a tuberculous affection, and that it belonged to the group to which the name "tuberculide" had been given. That was, he believed it to be due to a reaction of the skin to circulating tubercle bacilli. The fact that these lesions had healed he did not consider to be against, but rather in favour of the view. He had under his care a woman whom he had shown there, who had hundreds of small scars on the upper extremities, and some large scars, very similar to those in this case, on her lower extremities. He had followed that case for several years; she had had the eruption eight years. Every lesion healed up practically without treatment; she had usually had just a simple ointment given to her. In this type of case the lesions did tend to heal. Most cases of Bazin's disease could be healed by placing the patient for a few weeks in the horizontal posture. These cases were entirely different from scrofulodermia and some forms of lupus.

Dr. **Adamson** did not think this was a tuberculide condition. The patient had not the cold hands and feet that such cases usually had, and did not give a marked von Pirquet's reaction, as those cases always did. And he did not think that in tuberculide one got such big, deep scars as were seen in this case without the breaking down of deeply seated nodules, which were absent in Dr. Sibley's case. He was inclined to regard it as Dermatitis artefacta. The alternative seemed to be a persistent Erythema multiforme, such as Dr. Gray, Dr. Little, and others had shown, but the irregular shape of the scars seemed more in favour of an artificially produced lesion.

Dr. **Gray** did not agree with Dr. Adamson that this was Dermatitis artefacta. He thought it belonged to that group of cases which had been labelled "persistent erythema." This case was almost identical, except in the matter of degree, with that which he showed at the International Congress. The lesions were distributed in much the same way, and there was the same difference in the lesions on the upper and the lower extremities. In the upper limbs the lesions were not usually associated with extensive hæmorrhage into them, while those in the lower limbs were, and there was a tendency for the latter to leave large pigmented scars behind. The initial lesions in the present case seemed to be much smaller than those in his case. Some of them were small follicular papules, and there was a slight tendency in all of them to have a little central hæmorrhage. There was also a tendency for the lesions in the lower limb to get damaged and to break down and become infected. In his case he was never able to produce evidence of tuberculosis, and that was so here. He did not know what their ætiology was. He labelled his "persistent erythematous eruption." The microscopical picture of his case was a very intense sub-epithelial cellular exudate, with much necrosis.

Dr. **Graham Little**, answering Dr. Gray, did not think that this case could be regarded as Erythema multiforme. The patient mentioned by Dr. Gray was under his observation several years, and though she was practically never free from some lesion during all that time, there was never any scarring. He thought the presence of scarring presented a very important differentiation. He did not think such an amount of scarring would result from Erythema multiforme, whatever type it might be supposed to be. It was, however, very like a case he showed to the Dermatological Society of London some fifteen years ago. It was then classed as a doubtful tuberculous process. The eruption was on the arms, and five years afterwards she came with typical Lupus vulgaris, a sequel which might be regarded as a corroboration of the earlier diagnosis. The condition in the present case was evidently tuberculous.

Dr. PERNET could not conceive of any Erythema multiforme leaving scars of that sort. He was inclined to the opinion that the condition was of a tuberculous nature. Some forms of cutaneous tuberculosis might clear up spontaneously, to some extent at any rate. It was observed in Lupus vulgaris, which might partially clear up and leave scar tissue behind. Material from the elbow lesions should be injected into a guinea-pig as a test.

Dr. PRINGLE said that as he had expressed a rather definite opinion upon the case in the other room, he felt bound to repeat it there. It was to the effect that this was a tuberculous affection. To his mind, this patient presented several well-defined different types of tuberculous manifestation in the skin; he had verrucose tuberculosis on the knuckles, elbows, knees, and points of pressure; he had typical papulo-necrotic lesions of "acnitis" type upon the forearms: and, although he had not had the chance of observing him very closely, he thought he had tuberculides of the angiokeratoma type on the backs of the hands. With regard to the scars present, there was certainly nothing about them incompatible with the diagnosis of tuberculosis. He could show two cases at the present moment with distinct and emphatic tuberculosis of the skin, presenting absolutely similar scarring. He would like further to emphasise the very important point laid down by Dr. Sequeira, that tuberculous processes of the skin, even of intense severity, tended to spontaneous healing when the patient was kept at rest in bed and mild antiseptics applied. This man had admittedly been off work, presumably resting, many times during the last eight years. Those points established, in his own mind, a fairly firm diagnosis of multiple tuberculous manifestations on the skin. He could not conceive that any mere erythematous process would leave scarring of this depth and intensity, although he was familiar with the disease to which Dr. Gray had referred, which presented so close a resemblance in some respects to skin tuberculosis.

Dr. F. PARKES WEBER thought the cutaneous affection was probably tuberculous, due to the local presence of tubercle bacilli in the cutaneous lesions. He would, like Dr. Pernet, suggest that the Lister Institute be asked to inoculate some material from the lesions into guinea-pigs to see whether, in that way, the tuberculous nature of the lesions could be proved. In that way the Lister Institute recently succeeded in demonstrating the tuberculous nature of a hospital case under his care, sent to the hospital as a case of "chronic pyæmia," but which was really one of the nature of multiple "tuberculous gummata." He supposed that cutaneous tuberculous lesions like the present one (if it really turned out to be tuberculous) bore a relationship to subcutaneous chronic tuberculous abscesses ("cold abscesses") and "tuberculous gummata," analogous to that which tertiary syphilitic lesions of the skin bore to ordinary subcutaneous gummata.

The PRESIDENT said that the predominant opinion was certainly in the direction of tuberculosis, and he agreed with it. He thought that at the moment they lacked confirmatory evidence, and it was to be hoped that Dr. Sibley would give them the result of his further investigation of the case. Perhaps he would make a biopsy. The remarks which had been made clearly showed the importance of a case of this kind, and were helpful in many directions, one in particular, as indicated by Dr. Sequeira and confirmed by Dr. Pringle—viz., that tuberculous manifestations would, under certain conditions, heal spontaneously without treatment.

Dr. SIBLEY (in reply) said he was much obliged for the remarks which had been made, and he would do what he could to have a further investigation carried out.

Note.—A subsequent von Pirquet's test resulted in a marked positive reaction and distinct vesication.

Dr. J. H. SEQUEIRA showed *Sclerodermia occurring in a case of myxœdema while under thyroid treatment,* described on p. 34.

Dr. F. PARKES WEBER asked if the rarity of cases of this kind might not be used equally well as an argument that sclerodermia was not directly dependent on any disease or alteration in functional activity of the thyroid gland. There might, of course, be some indirect relationship between thyroidal activity and the various forms of sclerodermia.

Dr. SEQUEIRA, replying to Dr. Parkes Weber, said that there were on record cases of sclerodermia in which the thyroid gland had been completely atrophied, with symptoms of myxœdema. He could give the references to them, if desired.

Dr. A. M. H. GRAY showed for Mr. WILFRED TROTTER, a case of *recurrent Herpes zoster of the face with hemiatrophy.* The patient was a girl, aged 11 years, and gave a history of repeated attacks of herpes on the right side of the face since infancy. The attacks began when she was aged 1 year, and had recurred every two or three months since; each attack was preceded by headache and fever, but local pain was not a marked feature. All attacks previous to the present one had involved only the second division of the fifth cranial nerve, the lesions being limited to the centre of the right cheek and right side of the nose. In the present attack, however, the lesions present were two in number, distributed over the areas of the buccal and submental branches of the third division of the fifth nerve. Two other points were of interest: firstly, very marked pitted scarring was present at the site of previous lesions; and secondly, there was marked atrophy of the cheek on the affected side. There were no appreciable sensory changes in the skin of the face.

The child had had measles, chicken-pox and scarlet fever, but otherwise had been in good health. There was no history of tuberculosis or syphilis in the family. The mother had had thirteen other children, who were all alive and well, and had had no miscarriages.

There was no evidence of any disease—no enlargement of the tonsils, no adenoids, and no ear trouble; the teeth and mouth were in good condition and the child had never had any trouble with the eyes.

Dr. Gray added that cases of this type were of interest from two points of view: firstly as to ætiology, and secondly as to nomenclature. In this case the evidence appeared to point to the lesions being in the region of Gasserian ganglion and of an inflammatory nature. As regards nomenclature, he believed the case to be a true zoster and that it differed entirely from the cases of recurrent, irregularly bilateral herpes which occured around the mouth. The case was sent to Mr. Trotter as possibly due to some intracranial trouble; he would be glad if members could suggest any treatment which would stop these recurrent attacks.

Dr. J. H. **Sequeira** thought this type of case was of great interest, and it was undoubtedly a source of great worry to dermatologists. He presumed they must all have had cases of recurrent herpes from some unexplained cause, and he would like to mention two points which had occurred in his experience. In one case the small son of a medical friend had frequent recurrent attacks of herpes about the middle of the cheek, as in this child's case, and he was asked to see him. He prescribed simple remedies, but he could not suggest a cause for the recurrences. The affection was said to have been started by the child having been scratched on that part of the face. Apparently the slight trauma sensitised the area. Ultimately, the child had his tonsils and adenoids removed, and though that was two years ago, there had been no further attack of herpes. He therefore had cases of recurrent herpes sent to the ear and throat department with the view of having the naso-pharynx examined, and he also inspected the teeth for evidence of peripheral irritation. He thought peripheral irritation was important as a ganglionic lesion. In support of that opinion, he might mention the fact that he had a patient suffering from a small rodent ulcer on the lower part of the lobule of the left ear. Each time that patient had radium applied, she developed a patch of herpes over the mental area on the same side. As to the Gasserian ganglion being affected, he thought it was on record that hæmorrhage had been found there in herpes associated with pneumonia.

Dr. **Graham Little** did not know whether Dr. Sequeira thought as he did that this was febrile herpes. He did not think it was Herpes zoster. Recurrences in true Herpes zoster were infinitely rare. With regard to Herpes simplex, he had had a certain number of cases of what must be called Herpes simplex, occurring time and again in the same positions; Dr. Adamson had also reported some instances. One case of his was extremely interesting—in a man who had had recurrent Herpes simplex on the back of the right wrist, which had occurred again and again in the same position for ten years. This restricted localisation he did not think was against Herpes simplex, but the fact of recurrences was very much against Herpes zoster, and he thought the history in the present case was against it also. The pain here did not seem sufficiently severe;

it was more a febrile attack than a painful one. Herpes zoster involving the fifth nerve was almost always an exceedingly painful condition.

Dr. Pernet said that the difficulty in these cases was as to whether one was dealing with Herpes zoster or Herpes simplex (febrilis), and he agreed that this was probably not true Herpes zoster. Many years ago he published a case in the *Transactions of the Dermatological Society of Great Britain and Ireland*.* In that patient he carefully observed each attack. The lady had three attacks of herpes at intervals. It was a unilateral condition—one large group. He came to the conclusion then that it was a true recurrent Herpes zoster: it seemed to fit in with all the clinical characters of that disease. But the point he wanted to bring out was that he thought a peripheral cause might be a factor, and he suggested that the eyes, which had never been examined, should be investigated. The report was that she had uncorrected astigmatism. This was corrected by suitable glasses, and since then she had had no more facial herpes, a fact which seemed to point to the case having been one of Herpes simplex. Howbeit, up to the present time there had been no more recurrences.

Dr. Pringle thought that a very important, and, indeed, essential feature of this case had been somewhat neglected in the debate—namely, the marked atrophy of the parts. He pretended to only slight knowledge on such a subject, but he thought that the atrophy strongly pointed to the probability of some disease of the Gasserian ganglion being the origin of the visible disease, to the exclusion of a peripheral cause.

Dr. F. Parkes Weber said that in the present case, unless they thought there was genuine muscular atrophy, which he regarded as doubtful, there seemed to be no nervous complication of the herpetic eruption. If, however, in a future attack the patient were to develop facial paralysis or local anæsthesia one would then be bound to regard the case as being an example of "ganglionic Herpes zoster."

Dr. Adamson thought the scarring left by the herpes was in favour of it being Herpes zoster, although Herpes zoster very rarely involved the second division of the fifth nerve. He did not think that such scarring occurred after Herpes recurrens.

The President said that from the writings of Dr. Head, who published, in the seventh volume of Clifford Allbutt and Rolleston's *System of Medicine*,† some special observations on herpes, it was likely he would include this case as a zoster, at any rate, Herpes ophthalmicus was counted by him as a zoster. In the twenty-two cases which Head published of the trigeminal kind, he noticed that the greatest frequency was in the first division of the ophthalmic—namely, eighteen cases—while the inferior and superior maxillary were only two each. Therefore it was clear that the development in this case was one of the most unusual.

Dr. Eddowes suggested that a very careful examination be made of the teeth in the upper and lower jaw, and the jaw itself, and the ear on that side. Some years ago he "scored" by finding a young lady, who had apparently incurable neuralgia on the side of the face, had some indurated wax in the ear. He removed that, and her neuralgia was cured. Apparently slight causes of irritation in the ear sometimes caused much disturbance. He was glad to hear Dr. Sequeira mention the curious effect of radium applied to his patient's ear. The observation was valuable.

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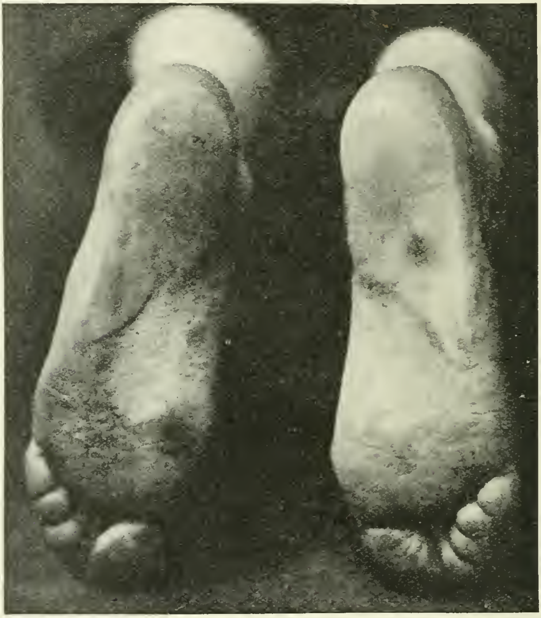
* Pernet, *Brit. Journ. Derm.*, 1897, ix, p. 151.

† Allbutt and Rolleston, *System of Medicine*, 1910, vii, pp. 470–492.

Dr. Gray (replying on behalf of Mr. Trotter) said the discussion does not seem to have included one of the important points—namely, the difference between Herpes zoster and Herpes febrilis. If one said that Herpes febrilis was a herpes which recurred, whereas Herpes zoster was a herpes which does not recur, the matter was simple; but he did not think that was the way in which one should define these cases. He looked upon Herpes zoster as a herpes which was produced as the result of a nerve lesion, whether in the ganglion or in a peripheral nerve, or, possibly, in one of the tracts of the spinal cord. He thought cases of Herpes simplex were probably due to local peripheral irritation of nerve endings; there was, as a rule, no restriction to nerve areas, and when they recurred they tended to do so more or less irregularly. The cases of herpes of the buttock which Dr. Adamson collected he would regard as Herpes zoster. Herpes about the mouth, preputial herpes, and possibly aphthous ulceration of the mouth he would put in the latter group.

Dr. George Pernet showed a *case of Morphœo-sclerodermia* (shown before*) *with recent acute symmetrical involvement of the soles of the feet.* A girl, aged 14 years, who was first seen at the West London Hospital on July 31st, 1914, for morphœic manifestations on the outer side of the right thigh, quite typical, but with a very diffuse lilac discoloration extending for some distance around (instead of the usual ring). Thickening followed, and this sclerodermia had progressed on the limbs in a symmetrical manner. This was demonstrated at the time the patient was shown before the Section on the first occasion. She was now brought forward again on account of an acute symmetrical involvement of both soles, which was observed on November 12th last. The parts shown in the photograph were at that time pale and somewhat swollen and œdematous, with a well-defined purple-lilac border. The affected areas were very tender and painful



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* *Brit. Journ Derm.*, 1915, xxvii, p. 286; *Proc. Roy. Soc. Med.*, 1915, viii (Derm. Sect.), p. 236.

to pressure. There was some hyperodrosis of the feet. Since then the pain on pressure had subsided to a great extent, and so had the swollen condition, giving place to a certain amount of toughness of the parts.

He considered the condition of the soles was part and parcel of the morphœo-sclerodermic process, but he would like to hear the opinion of members on this point. If he was correct in his opinion, then the case was a very unusual one. The patient had been on small doses of thyroid on and off since she was first seen. But the sclerodermia had advanced notwithstanding. She had had no arsenic.

The **PRESIDENT** did not see any connection between the condition on the soles of the feet and that on other parts of the body. He thought it was accidental. The patient had flat-feet and hyperidrosis, and also callosities, which might account for the pain. He thought there was a closer relation between the condition of the feet and the boots she wore.

Dr. **ADAMSON** said there was a good deal of leather-like thickening of the patches on the soles, and they had the sharp edge suggestive of sclerodermia. He thought the patches on the soles were probably an early state of sclerodermia.

Dr. **PRINGLE** was inclined to share Dr. Adamson's opinion. Seeing such a condition by itself, one would have classified it without hesitation as an example of Besnier's Keratodermia symmetrica or of Brooke's Erythema keratosa, but the onset of sclerodermia was sometimes so bizarre that the possibility of the condition of the soles in this case being of that nature forced itself upon one's consideration. He asked whether the patient had been taking arsenic as that was a frequent cause of a somewhat similar condition, but apparently she had not. He hoped the further progress of the case would be reported.

Dr. **PERNET** (in reply) said the affected portions of the soles had become harder the last week or two. He would try to keep her under observation and show her again if possible.

Dr. W. **KNOWSLEY SIBLEY** showed a case of *Actinomycosis*. The patient, W. J. T—, a restaurant caterer, aged 37 years, was sent to him by Dr. J. Bremner. He was stated to have had syphilis ten years ago, for which he was under treatment for two years. The patient spent a fortnight in September last at a house next a farmyard, at the foot of the Pentland Hills, Midlothian. He spent some time in the hay-fields, but he never handled any of the crops nor had he anything to do with the cattle. He first saw his doctor on October 20th, on account of a painless swelling that commenced on the inside and was then showing on the outside of the cheek. The doctor then removed two decayed stumps which seemed to have some connexion.

He presented himself at the hospital on November 25th, with a somewhat extensive irregular infiltration through the whole substance of the cheek, with a swelling the size of a walnut, which was felt and seen inside the mouth, and a nodular pustular eruption on the outside. A thick creamy pus was exuding from three or four points, which was found under the microscope to contain the ray fungus. The Wassermann reaction was negative.

Dr. PRINGLE thought that big doses of iodide of potassium would cure this case; but he believed that nothing less than a drachm a day would have a curative effect. He did not attempt to explain the *modus operandi*, but it was a widely accepted fact that big doses of iodides had a different effect from small ones, and that large doses were frequently better tolerated than small ones. He had an interesting experience of this disease which he had never before put on record.* He was called in consultation in September, 1898, by Dr. Tyson, of Folkestone, to see a gentleman, aged 59 years, who was suffering from ulcers of undetermined nature round the anus and on his face and right ear, which had appeared in the former situation in April of that year. These had been unsuccessfully treated by eminent surgeons with mercurials as being syphilitic. Subsequently a considerable portion of the lower end of the rectum and surrounding skin had been excised, and the condition was reported after microscopic examination to be indefinitely epitheliomatous. The lesions on the face and ear developed early in July, and, he had no doubt, were conveyed from the anal region by "picking," as the patient was difficult of control. When he saw him the ulcers about the anus had almost completely healed or had been removed by operation, but there was present on the centre of the chin a soft, boggy swelling as large as a walnut, the middle portion of which had broken down, leaving a deep crateriform ulcer, the base of which was bathed in bright sulphur-yellow granular pus, an impromptu microscopic examination of which at once revealed beautifully typical ray fungus. The pus from a similar ulcer on the antitragus of the right ear was of identical nature. The history of the case subsequently given by the patient was peculiar and interesting. He was a hunting man, and on one occasion late in the preceding season he had been attacked in the middle of a run with diarrhœa, and, after obtaining relief in a farm-yard, he had cleansed himself as best he could with a wisp of straw, shortly after which his trouble started round the anus. He did not think that there could be any doubt as to the cause and effect of this remarkable case. He might add that the patient recovered completely in about a year's time under iodide treatment, although it had frequently to be interrupted. He thought therefore, that he had some reason for his belief that the origin of Dr. Sibley's case was connected with his visit to a country farm, although many links were wanting in the chain of evidence.

Dr. EDDOWES said that he had had a case very similar to this, and managed to cure it very quickly. He made a strong solution of iodoform in sterilised vaseline, and injected it into all the sinuses, and he got the case well in a short time, without the internal administration of large doses of iodide of potassium.

The PRESIDENT said that a 1 per cent. solution of iodide of potassium was sometimes injected into the part with very good result, in addition to the general treatment.

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* The speaker refreshed his memory subsequent to the meeting by reference to his private case-book.—J. J. P.

Dr. **Alfred Eddowes** showed a *microscopical specimen for diagnosis.* A short time before a boy was brought to him with a small growth on his thigh about ¾ in. long. It was spindle-shaped, running in the direction of the limb. In the dull light of the out-patient room he thought it was Lupus vulgaris, but when he pressed it with a watch-glass there were no apple-jelly nodules to be seen. It was said to have been growing for two years, so he advised its removal. He took it out with a wide margin. It had been examined by two pathologists, but they are not sure as to the nature of it. There was a suspicion that it might be malignant. There was no glandular enlargement, and it had not the ordinary structure of Lupus vulgaris.

Dr. **Adamson** said that the microscopical appearances seemed to be those of a pigmented mole.

Dr. **Sequeira** suggested it was a nævus.

Mr. **McDonagh** thought it was an innocent endothelioma, or what was commonly called a "mole."

Dr. **Eddowes** (in reply) said that he was very much obliged to members for their opinions. There was no pigmentation observable, and he was now inclined to the view that it was a simple endothelioma.

Meeting held January 20th, 1916, Dr. J. H. **Stowers**, President of the Section, in the Chair.

Mr. J. E. R. **McDonagh** and Dr. H. **Spence** showed three cases of *syphilis treated by "intramine"* (*di-ortho-amino-thio-benzene*).

Case 1.—H. P—, aged 70 years, contracted syphilis in 1866, and had complained of a bad tongue for twenty-five years. The patient came to the hospital first eighteen months ago, when he had two intravenous injections of "606," which caused little or no improvement to the tongue condition. The salvarsan was followed by three courses of mercurial injections and iodides, which likewise produced no improvement.

On November 6th, 1915, the patient was given 1 grm. intramine intra-muscularly. At this time he exhibited an ulcer, the size of a sixpence, on the dorsum of the tongue, with two fissures running laterally from it. Posterior to the ulcer was a wart about the size of a small cherry. The movements of the tongue were restricted, and the patient suffered considerable pain and discomfort.

On the third day after the administration of the intramine the tongue began to improve, and when he was seen again a fortnight later, the ulcer had closed, the fissures had disappeared, and the wart was considerably smaller. At the present time (two months) the tongue had become soft and perfectly mobile, the wart had nearly disappeared, and the patient suffered no pain or discomfort; he said the tongue had never been so well for years.

Case 2.—J. W—, aged 42 years, contracted syphilis in 1898, and appeared to have had intermittent treatment during the following four years. The patient came to the hospital on December 20th, 1915, and gave a history of recurrent inflammation of the lower and central part of the face, that first appeared six years previously, and which would disappear under treatment after longer or shorter periods.

Upon admission the upper lip and the central half of the beard region, where now scarred, were dull and inflamed, and in places exulcerated; some bullous lesions were found on the right inner thigh, and a chronic laryngitis rendered him exceedingly hoarse.

On December 22nd he was given 0·4 grm. galyl, and on December 24th 1·5 grm. intramine intramuscularly. Six days later a considerable improvement in the condition of the face and also of the thigh was apparent, the redness of the face being distinctly lessened and the exulcerated lesions smaller or closed. On the eighth day all lesions were closed with the exception of a nummular area on the central part of the upper lip, which had now (January 20th) been healed a week. He had had two further injections of galyl, each 0·4 grm., on January 4th and January 11th respectively.

Case 3.—D. G—, aged 28 years, entered the hospital on November 27th, 1915, and was obviously a congenital syphilitic. The patient exhibited all the classical signs: the adenoid facies, flattened bridge, low brow, high arched V-shaped palate, chronic interstitial keratitis, together with partial destruction of the tongue, which was more or less fixed and could not be protruded. He was very deaf, speech was nasal, and there was a chronic disease of the naso-pharynx, and an odorous discharge, which was particularly marked upon admission to the wards. It was interesting to note that he furnished a history of exposure in the latter part of August, 1915, followed in four or five weeks by a "white pimple," which he scratched, the ulceration then spreading around the sulcus to the extent of one-quarter the circumference of the penis. Notwithstanding this circumstantial account the penile lesion upon admission exhibited the characters of, and was doubtless properly described as, a recurrent syphilitic one.

On November 30th, 0·35 grm. galyl was given, and on December 2nd 2 grm. intramine. Two days later the patient developed acute lobar pneumonia, the crisis occurring on the third day of the disease. Meanwhile the lesion in the sulcus had greatly improved, and upon discharge from hospital (December 29th) had practically closed.

Mr. J. E. R. McDonagh said that the cases which Dr. Spence and he had brought up had been exhibited, not so much with the idea of showing that a drug, not containing arsenic, had, if properly used, a stronger antisyphilitic action than salvarsan, but mainly to show what could be done in the way of finding new remedies for syphilis, once the rationale of chemotherapy was understood.

It was only by going from A to Z, or by dint of exhaustive perseverance without any logical guidance, that Ehrlich finally succeeded in discovering salvarsan. The reason why Ehrlich worked with arsenic was simply due to the fact that this drug had, as far as was known at that time, the greatest therapeutic action in sleeping sickness, for it would be remembered that it was to combat this disease that Ehrlich's work was primarily inaugurated. Ehrlich considered that salvarsan was parasitotropic and not organotropic, and that the arsenic was the toxophore group.

From his own researches it was perfectly clear that the arsenic in the salvarsan molecule does not attack the *Leucocytozoon syphilidis* directly, with the exception of the adult male phase and the female phase after impregnation, and these phases it was able to attack directly, owing to the free hydroxyl groups in their lipoid-globulin molecules.

Salvarsan, when administered, became attached to the lipoid-globulin molecules of the serum and of the plasma cells; therefore the drug was more organotropic than parasitotropic. Its influence was borne on the protozoal lipoid-globulin molecules only, owing to the increased size and adsorptive capacity of these molecules.

Salvarsan was adsorbed in virtue of its ortho-amino groups, and when adsorbed, the compound broke down and liberated the arsenic.

In his opinion, the arsenic became converted into a hydroxide and behaved in this respect like ferric hydroxide, the function of which was to form active oxygen. Active oxygen was required for the physical action of adsorption, which took place between the lipoid-globulin molecules of the serum and of the plasma cells and those of the parasites, with resulting destruction of the latter. This active oxygen was formed normally in the body by the action of ferric hydroxide, which was called a peroxidase, upon a peroxide, as in this equation

$$\text{R. Fe} + 4\ \text{H}_2\text{O} = \text{R. Fe} \quad \text{R. Fe}\ (\text{OH})_2 + 5\ \text{H} + 2\ \text{H}_2\text{O}_2 =$$
$$\text{R. Fe} + 6\ \text{H}_2\text{O} + \text{O}_1\ (\text{OH})_3 + 4\ \text{H} + \text{OH}.$$

The arsenic, then, in salvarsan acted simply as a peroxidase.

As the disease became more chronic the power of the host to form active oxygen directly decreased; consequently he was forced to form it indirectly, which he did by reduction.

As the result of some experimental work he found that metals acted as oxidising agents and non-metals as reducing agents; therefore it struck him that a non-metallic compound, provided that it was powerfully adsorbed, would increase the reducing action of the lipoid-globulin molecules in recurrent and in late syphilis, as salvarsan increased the oxidising action in early syphilis. Consequently he made several compounds of sulphur, and the compound which turned out to be the best was di-ortho-amino-thio-benzene, or, as he had called it for short, intramine. After adsorption the sulphur became free and acted as a disulphide, as in this equation:

$$\text{R. S}_2 + 2\ \text{H} + 4\ \text{OH} = \text{S} + \text{R.SH} + 2\ \text{H}_2\text{O}_2 + \text{H}^1$$
$$\text{R.(SH)}_2 + \text{S} = \text{H}_2\text{S} + \text{R.S}_2$$
$$\text{R.(SH)}_2 + \text{O} = \text{R.S}_2 + \text{H}_2\text{O}.$$

The disulphide protein produced active hydrogen and the peroxide necessary for the formation of active oxygen in the oxidase system.

From these few remarks they would see that intramine should be prescribed first in recurrent and in late syphilis, and a metallic compound after, while in early syphilis a metallic compound should precede the intramine. In fact, if intramine was prescribed before a metallic compound in early syphilis, it might occasionally aggravate the symptoms. This was due, he thought, to the avidity the mercaptan protein (R.SH) has for active oxygen, as seen in this equation:

$$2\ \text{R.SH} + \text{O} = 2\ \text{R.S} + \text{H}_2\text{O}.$$

He had shown them that day only cases treated with a non-metallic compound which contained no arsenic. At a future meeting he hoped to show them some cases treated with metallic compounds which contained no arsenic. He had already prepared some strongly adsorbed compounds of aluminium and iron, which, he thought, would replace the arsenical compounds altogether.

Arsenic was a poisonous metal, while the other metals just mentioned were not; and when, in conclusion, he stated that 12 grm. of intramine could be injected intramuscularly, and 8 grm. or more of aluvine and ferrivine (the new aluminium and iron compounds) could be injected intravenously without producing the slightest toxic symptoms, he thought they would agree that the statement made, to the effect that arsenic was not necessary, was a correct one.

Dr. G. PERNET asked if local reactions were produced in the muscles by intramine. Mr. McDonagh alluded to other metallic substances; some time ago antimony was experimentally tried, and though he did not want to anticipate his work, he supposed he was trying antimony.

The PRESIDENT thought they would all realise that this was a very important communication on the part of Mr. McDonagh on a subject in which they were deeply interested. They would look forward with pleasure to hearing him further on the matter in the course of a few weeks. It needed a larger knowledge of biochemical problems than he, personally, possessed at present to discuss such a subject as this. But two things were clearly needful: one was that they should understand the principles upon which the most efficient treatment of syphilitic diseases were based; and, secondly, they should, as far as possible, obtain for their patients the least toxic agents.

Mr. McDONAGH (in reply) said that whether there were local reactions in the muscles depended on how the substance were made; but the drug could be obtained. The patient might or might not have pain, but if there was pain it was not nearly so acute as that following the injection of salvarsan, or, at any rate, the pain that used to occur on injection in the early days of its use. It was absorbed in four or five days, and it did not form lumps. Antimony was the one metal which they could not possibly work with for this purpose; it was much too toxic; it was more toxic than salvarsan. And the reason it was unsuitable was that its atomic weight was too great. Intramine was on the market, and could be obtained from the British Drug Houses, Ltd.

Dr. E. G. GRAHAM LITTLE showed a case of *very extensive Tinea circinata of tropical origin.* The patient was a British soldier who lately arrived in London from West Africa. He had had gonorrhœa but not syphilis, and the Wassermann test was negative. The eruption began in the groin in September last, and had spread extensively until, as at the present time, the greater part of the body had become affected. The eruption consisted of (1) large ringed patches, the largest on the nape of the neck and left side of the cheek and the chin, where the ring was some 5 in. in diameter; and (2) eczematoid surfaces, resulting, no doubt, from the irritation caused by the disease. The abdomen, the scrotum, the thighs from pubes to ankle, the dorsum of the feet, the clefts between the toes, the sides of the chest, the sacral and interscapular regions on the back, the axillæ, the forearms, and backs of the hands, were involved in the eruption. The large ring on the nape had spread into the scalp, but there was no disease of the hair either there or in the pubic region. The nails were nowhere affected. The eruption had varied in severity, and under the mistaken diagnosis of psoriasis he appeared to have had some treatment with a chrysarobin ointment, under which it improved, as well as also under applications of iodine. The fungus was identified in scales taken from several parts of the body, and the mycelium was plentiful and coarse. An attempt had been made to grow the fungus on a Petri dish containing Sabouraud's maltose agar medium, but with no success, a common mould alone having been grown after a couple of weeks in the incubator. The exhibitor was obliged to Prof. Castellani for some hints for securing growth, and another effort would be made. The man travelled with the eruption fully developed from West Africa in company with four others who shared the same cabin, and they had not contracted the disease. The fact that the eruption began in the groin and had so quickly assumed the eczematoid aspect, and that it nowhere affected the hair, pointed to the probability that the organism responsible was the *Epidermophyton inguinale*, and if so this case was certainly the most extensive the exhibitor had seen or read of.*

Dr. E. G. GRAHAM LITTLE also showed a case of *chronic ulceration* in a boy, shown at the October meeting. This patient was shown again to illustrate the remarkable result of treatment by vaccines. A report was also made on the case at the November meeting,† when the boy was too ill to be shown. On November 15th the first dose was given of a vaccine derived from his own organisms, grown from the surface, which proved to be chiefly streptococcus and *Bacillus pyocyaneus*;

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* Specimens of the fungus in the scales were demonstrated after the meeting.

† *Proceedings* (Derm. Sect.), 1915, ix, p. 21.

5 millions of the former and 3 millions of the latter constituted the initial dose, and this was increased to 10 million of both organisms on November 21st. This dose was again repeated on November 29th. On December 5th, 10 million streptococcus and 20 million *pyocyaneus* were given, and the respective doses repeated on December 10th, and 10 million streptococcus and 25 million *pyocyaneus* given on December 16th. During this time continuous dressings of sanitas and baths with 5 per cent. saline were used, with a trial for a short time of a treatment consisting of painting the lesions with pure carbolic and swabbing the painted surface immediately after with absolute alcohol. Some improvement resulted from treatment with these vaccines, but no conspicuous success was in evidence until after December 20th. On this date a vaccine obtained from an organism which had been isolated from the blood by Dr. Colebrooke on November 25th was first given. Some time later films prepared from an unbroken bleb seemed to indicate the presence of the same organism, and this statement was made by the exhibitor, which he now wishes to correct, as further investigation made it apparent that this identification was erroneous. On December 23rd 5 millions of the new vaccine obtained from the coliform bacillus isolated from the blood were given, 7½ millions on December 25th, and 10 millions on December 27th. This latter dose was repeated on January 3rd, 10th, and 17th, and the patient was then discharged, completely free of any disease of the surface of the skin. Improvement was rapid and uninterrupted from the date of the first injection of 10 millions of the coliform vaccine, and as there was no synchronous change in any other detail of treatment, the improvement is attributable to the vaccine. There was considerable scarring of the affected parts, which, it would be remembered, were deeply ulcerated, but with this exception no trace of the disease remained. The temperature from start to finish had never been above 99° F., and had usually been subnormal. The pulse-rate in the earlier stages of observation (the patient had been under the charge of the exhibitor only from November 21st—up to that time he was in the Inoculation Department) was usually about 100, but had now settled around the rate of 80. The bowels had always tended to constipation, and at no time had there been any looseness or abdominal pain suggestive of colitis. The fæces, however, had not been examined.

A few days after the report of the exhibition of this case (in October) had appeared in the *Proceedings*, the exhibitor received a letter from Dr. Stacey Wilson, of Birmingham, who mentioned that on reading this report he identified the case as similar to a case which had occurred in his own practice several years ago. Dr. Stacey Wilson had been good enough to contribute the following account of this interesting patient. With this exception, he had been unable to find any analogue to this extraordinary case of his.

[*Note by Dr. T. Stacey Wilson.*—" I regret that the notes of the case I am about to record have been mislaid, and therefore the following description, being from memory, is not so full as could be desired, although it is substantially accurate, as its striking and unusual features were indelibly impressed upon the memory.

" The patient, a married woman, aged about 30 years, was admitted to the Birmingham General Hospital in a septicæmic condition, with a very extensive affection of the skin. Her temperature was moderately high, and she appeared to be dangerously ill. The skin affection varied in different parts of the body. One of the most remarkable types was an inflammatory infiltration of the subcutaneous and cutaneous tissues over the front of the chest, extending from about the second rib down to near the lower end of the sternum, and embracing almost the whole width of the chest. The infiltration was so great that this part of the skin stood some 1½ in. or more above its proper level. The raised area was of brownish colour, very hard, not œdematous, not specially tender on pressure. There were similar asymmetrical hard thickened areas on the thighs and parts of the back, and, I think, on one side of the abdomen.

" There was another type of eruption on, I think, the arms and legs, which may possibly have been an earlier stage of the one just described. These showed more distinct congestion, and were purple red patches which were apt to become vesicular and then ulcerate, as described by Dr. Douglas Heath.

" As regards the changes taking place in the above-mentioned infiltrated areas. In some instances—as in the case of the large shield-like area over the front of the chest—there was no definite change (other than a slight increase in its thickness) until resolution began to take place. In other parts of the body, however, a portion of a thickened area would commence to swell more than the rest, and then break down and ulcerate. These ulcerated areas were in one or two places as large as the palm of the hand. They did not seem due to a loss of substance, but rather to exuberant, fungating granulations bursting through the epidermis. Subsequently there was a certain amount of loss of substance, causing the ulcer to have a ragged, irregular surface. There was no unusual fœtor noticeable. This process of swelling and ulceration would take place in the course of a few days.

"The cause of this eruption was suggested by the appearance of the early stages of an infiltrated area which was watched carefully throughout the progress. The area affected was the back and radial side of the left wrist, and the adjacent parts of the hand and forearm. In this area congestion was first noticed with some sense of heat and pain. Then, in a day or so, all over the area small yellow points were noticed, due to small collections of serum, of the size of a pin's head and smaller—*i.e.*, the characteristic appearance seen in cheiropompholix. Then day by day the swelling increased, and the little collections of serum became less evident. In the course of a few days the area was raised to the extent of 1 in. or more above its normal level, and then the surface began to break down in places, and irregular masses of granulations were formed. The process went on until, at the end of a week or ten days from its commencement, a large part of the area spoken of was covered with ragged suppurating granulations. The appearance of the characteristic 'sago grain' collections of serum in the skin (as in cheiropompholix) pointed strongly to a blockage of the lymph vessels by inflammatory changes within them and to a collection of the serum in the intercellular spaces. This appearance was suggestive of an infective origin, and after several fruitless attempts the *Bacillus coli* was obtained in, I think, pure culture from the subcutaneous tissue.

"This case occurred before the days of vaccine treatment for ordinary diseases, and I therefore gave an effective general antiseptic, consisting of sodium sulphocarbolate in 20 gr. doses every two hours night and day, and 2 gr. of quinine every two hours alternating with it. In this way something over 90 gr., I believe, of pure carbolic acid, as well as the 24 gr. of quinine, were got into the system each twenty-four hours, and could be continued for weeks or months.

The only precaution necessary is to watch for the appearance of the muscular weariness on slight exertion which shows the physiological effect of carbolic acid. When this appears the dose must be lessened somewhat. A liberal ordinary diet was given with 6 oz. or 8 oz. of raw meat in addition. Under this general treatment, combined with local antiseptics, fresh areas ceased to become affected and the ulcerations commenced to heal. Later, the thickened areas began to disappear, and in the course of two or three months the patient left the hospital quite well and with but little sign of the widespread and deep skin eruption.

"The subsequent history of the case is of interest. A year or two later she came to the hospital again, but suffering from an extensive consolidation of the apex of the left lung. From this she made a good recovery in the course of a year or so. It was diagnosed and treated as phthisis.

"A year or two later she again presented herself at the hospital, looking extremely ill. She was in a septicæmic state, and it was found that there was chronic pelvic inflammation too extensive for operation. There were old sinuses discharging pus in the neighbourhood of the rectum, uterus, and bladder. The main organism in the pus was the colon bacillus. The patient was again admitted to the hospital, but did not live many weeks. Thus the question arises whether a pelvic inflammation caused by the *Bacillus coli* may not have been the source of the first infection."]

He wished to express his thanks for the courteous assistance he had received from Dr. Colebrook and Dr. Parry Morgan, of the Inoculation Department of St. Mary's Hospital, to whom all the credit of the investigation was due.

Dr. Colebrook's report was as follows: "Cultures taken from lesions (ulcerated) showed always many streptococci, usually also *Bacillus pyocyaneus* and staphylococcus. Cultures from unbroken blebs within a day or two of their appearance showed on one occasion staphylococcus and streptococcus, on another occasion sarcinæ and staphylococcus. Blood cultures: No. 1 was positive, yielding a bacillus; Nos. 2 and 3, taken a few days later, were both negative, 10 c.c. of blood being taken on each occasion.

"*Re* the positive blood culture: This was performed at a time (November 25th) when temperature was subnormal, but fresh lesions had recently appeared. The organism was obtained in pure culture from three of the seven tubes of broth into which the blood (10 c.c.) was divided.

"Character of the organism isolated: A bacillus with rounded ends, somewhat pleomorphic, but short forms predominate; some short chains have been seen. It was Gram-negative. Staining was uniform. Growth abundant on ordinary media, colonies being raised and opaque. On potato no brown coloration. Gelatine was liquefied slowly. Inoculation of culture into guinea-pig's peritoneum had given rise to no sign of illness (six weeks).

"*Note.*—This organism isolated from the blood had not been found in lesions, as was at first thought to be the case."

Dr. **Pringle** said that those who saw this patient when he was previously exhibited must be astonished at the remarkable recovery which had taken place. When the case was first brought to the Section, Dr. Pernet and he thought it might be a case of some form of pemphigus, possibly a "vegetans." He would like to ask Dr. Little whether the stools were also examined bacteriologically. He raised the point because he had recently had occasion to use vaccines made from various abnormal coliform bacilli found in the fæces in somewhat similar conditions, and with a success comparable with that which had attended treatment in this case, upon which he very heartily congratulated Dr. Graham Little.

Dr. **Douglas Heath** said that as he saw the case which had been referred to by Dr. Graham Little, which was under the care of his colleague Dr. Stacey Wilson, he might say that the skin lesions in that case when he saw it were not so severe as they were in the case under discussion. The eruption in Dr. Wilson's case resembled at first that of Erythema multiforme. The affected areas became deeply cyanosed and congested on the limbs, the lesions seeming to start from underneath the skin, and a few of them were bullous and slightly ulcerated on the surface. *Bacillus coli* was obtained from the breaking down areas. He believed there was some bowel trouble as well; perhaps Dr. Stacey Wilson's letter would refer to that. He knew sulphocarbolate of soda was given in big doses, but in that case when he saw it there was not the severe breaking down and the offensive odour observed in the present patient.* He had had at the hospital one other case of his own, a woman, aged 30 years, showing purple-red patches on the legs, and after a time bullæ appeared. The hospital bacteriologist obtained from it a coliform bacillus, such as he had not seen before, and cultivations from the bullæ yielded a coliform bacillus. In the bullæ was a creamy white pus. It disappeared readily under ordinary antiseptic treatment. He did not administer a vaccine. Careful sterilisation of the skin was carried out, so there was no contamination from without.

The **President** hoped they might look forward to a final report on this case.

Dr. E. G. **Graham Little** read a *note on the case shown for diagnosis at the last Meeting, of an Indian medical student of eruption which it*

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* He had since heard that more severe ulceration took place afterwards.

had been suggested by several members was tuberculous. The largest tumour, removed from the forehead, had been divided into two parts, and one part used for inoculation into a guinea-pig and the other part submitted for report to Dr. Spilsbury. The guinea-pig had shown no symptoms of inflammation at the site of inoculation, and had now been killed and an autopsy made five weeks after inoculation. Dr. Colebrook reported that there were no signs of tuberculous infection. As the disease, if tuberculous, was clinically of the nature of acute lupus, failure to infect the guinea-pig was, as far as it went, a contra-indication of the diagnosis of tubercle. Dr. Spilsbury reported of the section of the tumour that this was quite unlike tuberculous tissue, and that he conceived the possibility of leprosy, but sections stained for baccilli did not reveal the presence of any organism. The diagnosis at present offered was simply of a granuloma of unknown causation.

Dr. F. PARKES WEBER showed a case of *so-called idiopathic multiple pigment sarcoma of Kaposi* (*acro-sarcoma multiplex cutaneum telangiectodes of Unna*). This patient, who was born in Galicia of Jewish parents, was shown at the Dermatological Society of London on February 8th, 1905, and his case was described in the *British Journal of Dermatology* for April, 1905 (xvii, p. 135).* At that time he was aged 46 years, and presented the typical bluish nodules in the skin of the right foot, the left lower extremity, the hands, and the penis. In some of these parts, in addition to the bluish nodules, there were likewise small sessile or pedunculated outgrowths. There was also considerable chronic œdema of the left foot and ankle, such as was present in many cases of the disease. The illness was at that time of about three years' duration, and the prognosis (as was remarked in the description of the case) seemed not to be altogether unfavourable, "considering that the patient's general health is good, that the disease is probably seldom of itself fatal, and that in some cases improvement or spontaneous cure has apparently occurred after the disease has lasted twenty years or more."

The patient was for a time treated with arsenic, and for a time externally with lead lotion, but for the last four years he said he had

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* Some notes on the histology of the case were contributed by Dr. J. M. H. MacLeod to the *Brit. Journ. Derm.*, 1905, xvii, p 173.

had no treatment at all. He was now aged 59 years, and looked well and active. There was moderate œdema of both legs. The left lower extremity was still the more affected of the two. There were brown-red or purple patches on the feet and (much less) on the legs. On the feet and legs there were a few, small, dark-coloured, hard, cutaneous nodules, and there were a few on the thighs and glans penis, and there were one or two minute bluish nodules on the hands. There were now not any of the small pedunculated (pendulous) tumours. There was no evidence of any visceral disease, and the urine was free from albumin and sugar.

Dr. J. H. SEQUEIRA said that Dr. Pringle had asked him to say a word about the patient, also a Galician Jew, whom he first saw in 1888, and who died in the London Hospital from dilated heart secondary to bronchitis and emphysema two or three years ago. At one period the disease was in a grave state, and one leg was amputated, but the other leg cleared up entirely, and at the time of his death there was no sign of tumour.

Mr. T. P. BEDDOES said that a case similar to this was under his observation for some years, and was of interest from its duration. It started about twenty-one years ago, under Dr. Wyndham Cottle, the patient continually having pedunculated growths, mostly below the knees. These healed up for a time and under treatment, but recurred and fresh ones formed which ulcerated, and finally the only diagnostic point about which there could be no doubt was one spot on the forearm which was only slightly raised. In the course of twenty years considerable œdema formed about the limbs, with gangrene. He did not see the patient for about two months before the end, but considered that the condition was a good deal associated with age—he was 75 when he died—and that, if it had not been for kidney trouble and heart trouble, his case would have been looked upon as favourable. At no time did the pigmentation disappear, and, during the years he had seen him, the pedunculated growths, which ulcerated, were never absent. Members of the Section might remember that he showed a case both here and at the International Congress of Medicine, which was generally looked upon as of a similar nature. But the patient was younger, the growths were more vivid, grew more rapidly, and there was, as in this case, ulceration of the penis.

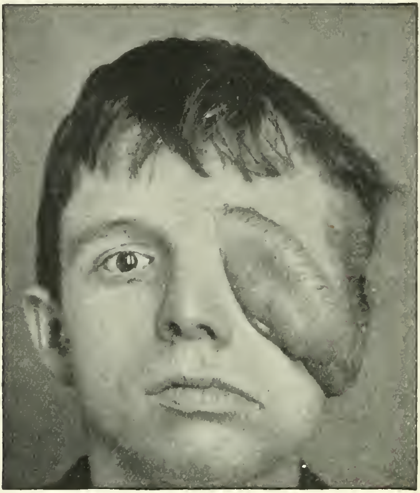
Dr. GORDON WARD showed a case of *tertiary syphilide*. The patient, a male, aged 37 years, previously a stoker and now a soldier, had a primary sore sixteen years ago, and present rash appeared at or about the same time. It had never caused any trouble or interfered with his work as a stoker. It had been treated on different occasions as a syphilide, but without improvement. The patient stated that the eruption was markedly better in winter and worse in summer, and that it had never given rise to irritation. There had been no itching at any time. There was no eosinophilia. The general health was not affected, and there was no history of any change in type of the disease. The patient had had no other serious illness. There was no relevant family history, and he had not been abroad.

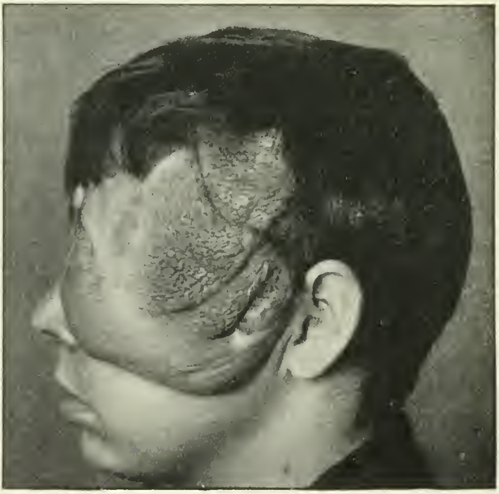
The lesions were most typical on the back and consisted of papules with scaly tops at the periphery and pigmented patches more centrally. These papules were, in some cases, surmounted by flat yellow vesicles which dried quickly, leaving scales. Fluid from mall bullæ only showed degenrate leucocytees and staphylococci. Scales showed many clusters of yeast-like organisms but no mycelium.

This case was shown to elicit answers to the questions: (1) What was the diagnosis? (2) Was the man fit for general military service overseas?

The PRESIDENT did not think any member would differ as to the diagnosis. There was no doubt the case is syphilitic. The point of interest was: what treatment has been applied, and what should now be adopted? Intravenous injections of galyl, or the like, were indicated, and intramuscular injections of mercury at intervals subsequently. He had seen several cases lately which had impressed him very much as to the lenient manner in which men were let off military duty for comparatively trivial ailments. He did not think this patient should be unfit in a couple of months to do what was required of him as a soldier.

Dr. S. E. DORE showed a *case for diagnosis.* The patient was a male aged 40 years. He brought this case at the suggestion of his surgical colleague, Mr. Rock Carling, under whose care he was admitted to Westminster Hospital three days before. The patient had just come from France, where he was at a military hospital in Rouen. This was one of a number of cases of dermatological interest which were being sent from the Front, and one of the important points was that, according to his own statement, eight out of seventeen patients in the same ward suffered from the same complaint. The history was that the affection began six weeks ago on the right hand with an eruption of papules and vesicles which subsequently became bullous, and the dorsal surface was now covered with bullæ and excoriations. A week ago the left hand and elbows became affected in a similar manner, the lesions also becoming bullous, and three days ago the eruption began to appear in the form of erythematous patches on the feet. His view of the case was that it was a streptococcic impetigo, but some circinate erythematous patches, with dark centres, on the feet suggested the diagnosis of Erythema iris.





TO ILLUSTRATE DR. J. H. SEQUEIRA'S CASE OF DERMATOLYSIS AND MOLLUSCUM FIBROSUM.

Dr. A. **Eddowes** suggested that when the history was carefully taken it would show that this was a condition with which they are fairly well acquainted in the out-patient departments of hospitals. A little itching began between two toes; the condition was neglected; toxins accumulated in company with the organisms themselves, and then extended to other parts, producing a so-called eczema rubrum. He looked upon this infection as probably streptococcic mainly, with perhaps some addition of *Staphylococcus albus* infection *Staphylococcus albus* was often a very vigorous organism, causing blistering. It might be carried from one leg to the other by socks, to the hands by washing, and on to the projecting parts by drawing on the pants, etc., and took most effect on the points most subject to pressure and friction.

The **President** hoped that Dr. Dore would give them a further report on this case. The possibility of septic pemphigus was not to be forgotten.

Dr. J. H. **Sequeira** showed a case of *sclerodermia with Graves's disease*, reported in detail on p. 33. The case was shown as a contrast to the patient exhibited at the last meeting, in whom sclerodermia developed in a myxœdematous patient while taking thyroid extract.

Dr. **Travers Smith** said the connection between Graves's disease and sclerodermia was of great interest to him. He had under his care a whole family which showed this relationship. The father had sclerodermia, exophthalmos, and some valvular trouble of the heart; his daughter had Raynaud's disease and had lost the ends of several fingers, and had ulcerations in various parts of the body; two children, aged 12 years and 8 years, had enlarged thyroids, some prominence of the eyeballs, and slight tachycardia. They were exhibited at a local medical society in Kilburn. The father died of syncope. He had not ordinary valvular disease, because at times he seemed to be quite free from symptoms, the main character of which was a rapid and tumultuous action of the heart.

Dr. F. **Parkes Weber** said that cases like the present one, which proved the occasional association of sclerodermia and Graves's disease, suggested that, as he remarked at the last meeting with regard to Dr. Sequeira's case (of sclerodermia and myxœdema), there could not be any *direct* connection between myxœdema and sclerodermia; if there was any connection at all between the last two diseases, it was only an indirect one.

Dr. A. **Eddowes** said that this was another instance of a long list of cases of sclerodermia beginning over the left clavicle.

Dr. J. H. **Sequeira** showed a case of *dermatolysis and Molluscum fibrosum, with congenital morbus cordis and kyphosis*. The patient, an undersized youth, aged 21 years, who looked more like a boy aged 15 years, was born in Yorkshire. He presented a remarkable, soft, pendulous growth on the left side of the forehead. The tumour hung down over the orbit and cheek. The surface in the lower part had the appearance of the adjacent skin, while on the scalp it had a peculiar corrugated character resembling the skin of the scrotum. The left eye was removed some years back for the condition known as buphthalmos. On the trunk, particularly on the back, were numerous molluscum tumours the size of small nuts. They had a bluish tint, and on pressure could be herniated under the adjacent skin. The patient had congenital kyphosis of the lumbar spine, with compensatory curvations in the dorsal region, well shown in a skiagram exhibited. He had also congenital morbus cordis, the defect being, in the opinion of Dr. Robert Hutchison, at the aortic valve. He proposed to ask one of his surgical colleagues to see the lad, with a view to operative treatment of the facial deformity.

The frequent association of congenital anomalies was pointed out long ago by Dr. Francis Warner. The head tumour resembled some of the cases of dermatolysis which had been published, while the growths on the trunk were characteristic examples of Molluscum fibrosum.

Dr. F. PARKES WEBER ventured to suggest that the so-called dermatolysis tumour about the patient's left eye belonged really to the class of plexiform neuroma, although he admitted that he could not feel any distinct bands of plexiform neuroma in it. If he was right, then in the present case they had the typical trio of von Recklinghausen's disease—namely, plexiform neuroma, molluscum fibrosum, and spots of cutaneous pigmentation on the back and trunk.

ERRATUM.

Vol. xxvii. No. 326, p. 471. Fifth line from bottom in report of Dr. Pernet's case "strong" should read "stony."

THE FOURTEENTH ANNUAL REPORT OF THE INSTITUTE FOR MEDICAL RESEARCH, KUALA LUMPUR, FEDERATED MALAY STATES, 1914.

THE report contains a record of work which is of considerable dermatological interest, as it is mainly concerned with experiments on leprosy.

FISH AND LEPROSY.

A series of experiments were carried out with the object of deciding the so-called fish hypothesis of leprosy, and whether decomposed fish could be incriminated as a source of infection.

If the fish theory were true, then the organism of the disease would be expected to exist in a living state and to proliferate in some form of putrid fish; but even if it did so, the cultivation of an acid-fast bacillus from putrid fish would be inconclusive evidence, as there would be no means of identifying the bacillus, and the ubiquitous distribution of acid-fast bacilli is well known.

There seemed little likelihood of the disease being conveyed by fish eaten in the cooked state, as the natives either fried it thoroughly in oil or roasted it until it became brittle, which procedures would destroy the bacilli. Consequently the fish media were entirely prepared from several types of preserved fish, such as dried salt fish, sharks' fins, cuttle fish, fish roes, dried prawns, fish pickled in brine, and various shellfish, which were favourite articles of diet among the Malays, Chinese, and Tamils, in the Malay States.

Media, composed of a paste made from one or other of these varieties of preserved fish, mixed with powdered agar and distilled water, were inoculated with nodules of leprous tissue. In every case the results were negative, and even at the close of a year no culture of the lepra bacillus could be detected in any of the tubes which had been inoculated.

Leprosy in Animals.

During the year under review twenty-five inoculation experiments with leprosy were performed in rabbits, guinea-pigs, rats, cocks, toads, and six Chinese freshwater fish. The results obtained were invariably negative.

Leprosy and Kedrowsky's Bacillus.

Of the various reported successes in cultivating the bacillus of leprosy that of Kedrowsky had attracted most attention, as Bayon has claimed to have confirmed his work, while in most other instances where the bacillus was said to have been grown, subsequent attempts to obtain a culture on the same medium have given negative results.

In 1900, from three cases of leprosy, Kedrowsky cultivated organisms which he believed to be related to the acid-fast bacillus found in leprous tissue. From two of the cases he isolated diphtheroids and from the third a non-acid-fast streptothrix. These he considered to be variations of the lepra bacillus which he regarded as being polymorphous. A rabbit which he inoculated intra-peritoneally with the streptothrix became gradually thinner and developed paralysis of the hind legs, and when it was killed six months later numerous tubercle-like nodules were found in the peritoneal cavity, liver, spleen, etc., in which were acid-fast bacilli. From this he recovered a culture of an acid-fast bacillus and various diphtheroids which were pathogenetic to rabbits and mice.

From a fourth case of leprosy he cultivated a diphtheroid similar to that from the above rabbit, which was also pathogenetic in rabbits.

From material obtained in London, Bayon cultivated an organism which he claimed to be identical with that of Kedrowsky.

With the object of confirming these findings, material abundant in acid-fast bacilli was excised from fifty-two cases of leprosy at Kuala Lumpur and inoculated on the medium employed by Kedrowsky and Bayon. In certain cases cultures of diphtheroids and streptothrices were obtained, while in others no growth appeared; but as the results were positive where the inoculated tissue was broken down and negative where the nodule had not begun to soften and was carefully excised, it was concluded that the organisms obtained in cultivation were merely contaminations, and that there was no evidence that the acid-fast bacillus of Kedrowsky was the lepra bacillus.

The Wassermann Reaction in Leprosy.

Experiments carried out with a view of determining the relation of the Wassermann reaction to leprosy gave uncertain results. There appeared to be no clinical criteria by which one could foretell the results. Certain tubercular and anæsthetic cases reacted positively, while others, clinically similar, did not. It has been suggested that the determining factor in the positive cases was latent syphilis, but although a certain number of the patients admitted antecedent syphilis, any examination of the nodules for the *Treponema pallidum* invariably gave negative results. It appeared that the positive Wassermann reactions were due to some other cause than syphilis.

J. M. H. M.

CURRENT LITERATURE.

ANTHRAX.

AN OUTBREAK OF ANTHRAX CONVEYED BY INFECTED SHAVING BRUSHES.

Reginald R. Elworthy. (*Lancet*, January 1st, 1916, p. 20.)

An account is given of three cases of anthrax in which the infection was conveyed by means of shaving brushes. These are the first recorded instances of this means of contracting the disease. Two of the cases survived, whereas in the third the disease proved fatal. A clinical record of the last case is given, as well as a detailed description of the bacteriological methods employed in proving that both used and unused shaving brushes from the same source were infected with anthrax bacilli. S. E. D.

A FATAL CASE OF ANTHRAX: INFECTION BY A SHAVING BRUSH.

E. H. Snell, with clinical notes by E. W. G. Masterman. (*Lancet*, January 29th, 1916, p. 242.)

The patient had been employed as a wood turner in an aeroplane factory, but no association could be traced between the man's disease and his occupation or his home surroundings. The writer hearing that some cases of anthrax had been traced to the use of shaving brushes, made inquiries and found that a shaving brush had been purchased from a local firm. Half a dozen of the same make, together with that used by the patient, were purchased and sent to the laboratory of the Local Government Board. The shaving brush of the deceased contained anthrax spores, but four of the other brushes were examined with negative results. Seven further brushes were then examined, and at least two of these contained virulent anthrax spores. S. E. D.

LEPROSY.

PRELIMINARY NOTE ON THE USE OF GYNOCARDATES ORALLY AND SUBCUTANEOUSLY IN LEPROSY.

Sir Leonard Rogers. (*Lancet*, February 5th, 1916, p. 288.)

On account of the nauseating properties of chaulmoogra oil and its interference with digestion, the writer has for a number of years prescribed gynocardic acid (also known as chaulmoogric acid and believed by many to be the active principle of the oil) in cases of leprosy. In three patients who had been able to tolerate large quantities of gynocardic acid by the mouth remarkable improvement took place in the course of a year or two of such treatment. Nastin was also used in these cases, but a careful trial of this drug alone in the Gobra Leper Asylum at Calcutta convinced the author that it was nearly, if not quite useless. Dr. Heiser having reported promising results from intra-muscular injections of chaulmoogra oil the author then tried the gynocardates in the form of an injection. The sodium and potassium salts proved to be readily soluble in water and were not changed during sterilisation by heat or by the addition of ½ per cent. carbolic acid for their preservation. The potassium salt dissolved more readily but was less convenient on account of its buttery consistency. The gynocardates gave the typical reaction of chaulmoogra oil with sulphuric acid—a brown colour changing to green—but leprolin gave no trace of the reaction and is thus probably useless. At first an impure preparation of sodium gynocardate was used and doses of only one or two grains were administered, although this produced distinct improvement in nearly all the cases in the first three months. During the last three months since a supply of the pure drug has been obtained the doses have been increased up to a maximum of four grains once or twice a week.

The author gives several instances to illustrate the results obtained. He considers that although it is too early to foresee the ultimate result of the treatment, the improvement in a number of cases of both anæsthetic and tubercular leprosy has been far more rapid than that obtained from any other method he has tried, including nastin subcutaneously and chaulmoogra oil and gynocardic acid by the mouth. S. E. D.

RECENT DEVELOPMENTS IN THE TREATMENT OF LEPROSY

VICTOR G. HEISER. (*New York Med. Journ.*, February 12th, 1916, p. 289.)

In this communication the author gives an account of the treatment of leprosy in the Philippines. At one time the X-rays seemed to warrant the belief that a cure for the disease had been found. Some cases remained negative, both microscopically and clinically, for a period of about a year, but later all relapsed. Nastin did not prove of value after repeated trials even when used over long periods of time. Salvarsan has been reported upon favourably, but seeing that over 50 per cent. of the cases gave positive Wassermann reactions it is apparent why improvement may occur. Many of the lepers also suffered with yaws, which also gives a positive Wassermann reaction and yields readily to salvarsan. Moreover, there is much reason to believe that frambœsia occurs in three stages like syphilis, and that in the third stage the lesions and deformities are often mistaken for those of leprosy. In view of these facts, it would appear doubtful whether salvarsan is of any value in uncomplicated leprosy. Vaccines have apparently caused improvement in some cases, but in the writer's experience they have not stood the test of time. Chaulmoogra oil is constantly mentioned in the history of the disease as being of value, but on account of the great nausea produced when it is taken by the mouth few patients could be induced to follow up the treatment for more than a few months, and it was estimated that only about one patient in three hundred could take it continuously for the required period of two years. For a time it appeared that the use of antileprol, which is said to be ordinary chaulmoogra oil from which the emetic principle has been extracted, might solve the problem, but the results were unsatisfactory. A review of the literature shows that chaulmoogra oil has been used hypodermically, but in the author's experience it was not absorbed after injection, and to overcome this difficulty it was combined with camphor and resorcin in the proportion of 60 c.c. of chaulmoogra oil, 60 c.c. of camphorated oil and 4 grm. of resorcin, this mixture being dissolved on a water bath and filtered. The injections are made into the buttocks at weekly intervals beginning with 1 c.c., which is gradually increased to the point of tolerance according to the reaction produced. Quicker results are obtained when the injection is made into large leprous deposits or in divided doses into smaller infiltrations. No strychnine is administered, but saline purgatives are freely employed, and 2 per cent. sodium carbonate baths are prescribed every other day. In discussing the diagnosis the writer lays great stress on the nasal ulcer which he considers to be the earliest and most constant symptom. It is situated on the septum at the junction of the cartilaginous and bony portions. This ulcer was noted in 75 per cent. of a series of 1200 cases, and the author's examination of more than 10,000 lepers confirmed the importance and constancy of this sign, bacilli being found after scarification and staining.

With reference to the results obtained from the treatment, the author states that five cases were reported as apparently cured and having remained cured for a period of over two years up to October, 1914, and recent advices from Manila state that twenty-three more lepers have been discharged from the leper hospitals as cured. In March, 1915, there were probably 200 more cases showing noticeable improvement. The author does not claim that a specific for leprosy has been found, but considers that more consistently favourable results are obtained from this than from any other method; moreover, the treatment is apparently equally efficacious in the tubercular, anæsthetic, and mixed varieties of leprosy.

S. E. D.

TROPICAL GRANULOMATA.

A CASE OF ORIENTAL SORE TREATED BY ANTIMONIUM TARTARUM (TARTAR EMETIC) LOCALLY. George C. Low. (*Journ. Trop. Med. and Hyg.*, 1915, xviii, p. 258.)

In this contribution good results are recorded in a case of Oriental sores due to *Leishmania tropica* from applications of an ointment containing 2 per cent. of antimony tartarate applied night and morning. J. M. H. M.

THE TREATMENT OF ULCERATING GRANULOMA OF THE PUDENDA. F. Terra. (*Boletim da Sociedade Brasileira de Dermatologia*, 1914, pp. 17 and 83.)

Dr. Terra records two cases of ulcerating granuloma of the pudenda, one of two years' and the other of twelve months' duration. The clinical aspects were characteristic, and in the scrapings Donovan bodies were found in the interior of the large cells, and also extra-cellular. Trixidine, a preparation of antimony, was injected intramuscularly, in view of the good results obtained in Leishmaniasis. The result was not satisfactory, and intravenous injections of tartrate of antimony were given with success. Dr. Werneck Machado (*ibid.*, pp. 35 and 83) presented cases similarly treated. In the discussion the antimony treatment was described as specific, but it was pointed out that to prevent recurrence the injections should be continued for a month after the disappearance of the lesions.

The intravenous injections consisted of 1 per cent. of tartrate of antimony in sterile physiological salt solution, the dose being 5 to 10 c.c. In long-standing cases ten injections may be required. J. H. S.

OCCUPATIONAL DERMATOSES.

SOME NEW FORMS OF OCCUPATIONAL DERMATOSES. R. PROSSER WHITE. (*Lancet*, February 19th, 1916, p. 400.)

THE author reports examples of dermatitis among workers in trinitrotoluene, nitrate of ammonium, and nitro-glycerine. Trinitrotoluene dermatitis begins as a superficial erythema, but as usually seen consists of patchy, irregular-shaped, slightly raised areas of redness, varying in size from a pin-head to a shilling, which coalesce by spreading at the edges and by the formation of new centres. The parts most affected are the hands and arms, the neck, the lower part of the abdomen, the inside of the thighs and scrotum, the back above the buttocks, the calves, and between the toes. The eruption may develop into a continuous sheet of redness or lichenification, vesication, pyogenic infection and superficial ulceration may occur. Desquamation depends upon the severity of the inflammation and the thickness of the epidermis; crusting is slight. The larger number of cases came from amongst the workers who sieve the fine powder; the other workers affected were employed in the same sheds, filling the fine powder into tins with scoops.

That the trinitrotoluene is the irritating agent was proved by the author by experiments upon himself and by the fact that no case of dermatitis occurred in any of the mixing houses where trinitrotoluene had been absent from the ingredients sieved. Nitrate of ammonia may give rise to a dermatitis under special conditions of temperature, subdivision, and predisposition. The rash is in the earliest stage a faint erythema. There was intense itching in two cases, but both were slight, and the men were never invalided from work. Any sore or crack into which the nitrate of ammonia gains access causes smarting. One case of stomonal dermatitis was observed. The powder causes severe smarting wherever it touches the skin, and, according to the patient's statement, burned holes in the glove worn to protect the right hand. The rash was situated upon the right hand, forearm, and neck. In the early stage it is erythematous, but later presents the appearance of Eczema rimosum, with deep fissures, especially on the fingers, thumb, and outer edges of the right hand. The writer describes the measures which should be taken to prevent these various forms of dermatitis, and also the methods of treatment he has found most useful.

The paper concludes with examples of "Conditioning" dermatitis and "Wet Winders'" acroasphyxia. S. E. D.

FUNGUS INFECTIONS.

A CUTANEOUS LESION CAUSED BY A NEW FUNGUS. G. G. LANE, M.D. (*Journ. Cut. Dis.*, 1915, xxxiii, p. 840.)

THE lesion, which resembled tuberculosis of the skin of the verrucose type, occurred in an Italian, aged 19 years, living at East Boston, and was present on the right buttock. It was excised under a local anæsthetic, and the provisional diagnosis of Blastomycosis was made from microscopical examination of the tissue. A second lesion appeared and was also excised. A fungus was found in the tissue which was grown on various media and inoculated into guinea-pigs. The cultural characteristics appeared to be somewhat different from the usual growths of the blastomyces.

The fungus appeared in the tissue in two forms: (1) A sclerotic cell, from 8 to 15 microns in diameter, round or oval in shape, with a brownish-black cell wall enclosing finely granular protoplasm with an occasional fat-drop; and (2) a budding form in which conidia were present.

The fungus grew on culture media as a branching septate greyish-brown mycelium, with hyphæ which were fairly straight and cylindrical on cross-section. The reproduction was asexual and took place in two ways: (1) Conidial formation by budding from sclerotic cells, as in the tissues; (2) semi-endogenous conidial formation by budding from specialised sporogenous cells on aerial hyphæ.

The fungus was not pathogenic for guinea-pigs. In rats and mice it produced a chronic skin lesion similar to that in man, and intra-peritoneal inoculation caused extensive tubercle formation in from four to eight weeks.

The fungus was submitted to Prof. Thaxter, of the Botanical Department of Harvard University, who considered that it was probably the type species of a new genus, and should be grouped with blastomycosis, sporotrichosis, under the "Fungi imperfecti."

J. M. H. M.

NEW GROWTHS.

PRE-CANCEROUS DERMATOSIS. J. T. Bowen, M.D. (*Journ. Cut. Dis.*, 1915, xxxiii, p. 787.)

In 1902 Bowen described two cases of epithelial proliferation of a peculiar type in which the lesions appeared as papules or tubercles, slightly elevated above the normal skin, of a moderately firm consistency, dull red in colour, and the surface of which was slightly crusted or papillomatous. The lesions either became confluent, forming areas of tumour-like masses, or remained discrete, or assumed annular or serpiginous figures. They showed no tendency to disappear spontaneously, and when they were removed by the curette or by freezing, new elements might appear at the periphery of the area in which the lesions had been destroyed.

Histologically there was a marked proliferation of the prickle cell layer, peculiar clumping of the nuclei and vacuolisation of the prickle cells, and more or less marked hyperkeratosis with here and there imperfectly cornified cells of the type of the "corps ronds" described by Darier in connection with Psorospermosis follicularis vegetans. The changes in the corium were constant and consisted in dilatation of the superficial capillaries, which were surrounded by a dense cellular infiltration chiefly composed of plasma cells. There was either an absence or a diminution of the elastic fibres in the corium of the affected area. The histological appearances thus showed a striking analogy to those in Paget's disease, a pre-cancerous condition.

In this contribution Bowen's two original cases are again recorded, and four additional ones, namely, two by Darier, one by Darier and Danel, and a fourth by Bowen. The writer concludes that these cases constitute a distinct type of disturbance not hitherto recognised, which he believes to be of a pre-cancerous nature. He considers that probably the cases are not so uncommon, as they might readily be missed by being mistaken for syphilis.

In 1900 Darier proposed the name "Dyskératose" for this type of epithelial growth, and included under the heading: (1) Psorospermose folliculaire végétante (Darier's disease); (2) Paget's disease of the nipple; (3) Molluscum contagiosum; (4) the pre-cancerous dermatosis of Bowen.

In all of these lesions there is a vitiated type of keratosis, in which cells of the "corps ronds" variety are met with.

So far, definite malignant changes have not been known to follow Molluscum contagiosum or Psorospermosis follicularis vegetans, but in this affection Darier has described malignant changes in a neighbouring gland.

J. M. H. M.

THE USE OF MERCURY IN VERRUCÆ PLANÆ JUVENILES.

Charles J. White. (*Journ. Cut. Dis.*, 1915, xxxiii, p. 738.)

In this contribution the writer describes a series of cases of Verruca plana juvenilis in which the warts were apparently cured, and cured quickly, under the internal administration of mercury, the drug being given in the form of protoiodide of mercury pills, one quarter of a grain *t.d.s.* J. M. H. M.

GENERAL PATHOLOGY.

THE RELATION OF INTERNAL SECRETIONS TO CUTANEOUS DISEASE.

O. H. Foester. (*Journ. Cut. Dis.*, January, 1916, p. 1.) E. M. McEwen. (*Ibid.*, January, 1916, p. 15.)

In the January issue two important contributions on the relation of internal secretions to cutaneous disease appear by Foester and McEwen respectively. Neither of these contributions lend themselves to abstraction, but must be read carefully *in toto* to be followed. In the former there is a good summary of the present state of our knowledge of the subject.

McEwen concludes that a direct or indirect relationship may be considered as existing or possible of existence between the endochrenous glands and the following skin-diseases: The pigmentation of Addison's disease, very probably the pigmentation from pregnancy and pelvic tumours, and pigmented new growths of the skin; the dermatoses which are persistently associated with diabetes; the dermatoses which are secondary to excess of body fat, both local and general; skin disturbances which are characteristic of puberty in both sexes as well as those which attend the involution of sex life; hypertrichosis in women; alopecia in certain instances in both sexes; dermatoses ætiologically related to hypo- and hyper-activity of the glands of the skin. J. M. H. M.

PHOTO-THERAPY.

FROM THE VISIBLE TO THE GAMMA RAY SPECTRUM.

Sidney Russ. (*Brit. Med. Journ.*, January 22nd, 1916, p. 124.)

A chart is given representing the wave lengths of rays ranging from the visible part of the spectrum to X-rays and the gamma rays of radium. The limit of visibility at the red end of the spectrum is 7594 tenth-metres, that is, ten thousand millionth parts of a metre; the visible region of the spectrum is constituted by almost one octave of radiation, and in the ultra-violet portion rather more than two octaves have been investigated. The author puts forward a plea for a more exact specification of the different types of radiation which are used in experimental investigations and therapeutically, and suggests that a statement of the range of wave lengths would eliminate many of the uncertainties introduced by such terms as "hard," "medium," and "soft" rays. With regard to the "unmapped" portion of the spectrum, which comprises about six octaves, separating the extreme ultra-violet from the softest X-rays, the interesting suggestion is made that these uninvestigated radiations, which are very easily absorbed by matter, play some part in the reactions of tissues when the latter are exposed to X or radium rays, and may explain the difference in the reaction of the skin to soft and hard rays of equal intensity. In referring to the dangers of X-rays, the writer insists that the introduction of deep X-ray therapy and the use of highly penetrating rays calls for a reconsideration of the methods of protection, and points out that hard X-rays have a penetrating power so high that the intensity of a beam is only cut down to 10 per cent. by passing through 12 or 13 cm. of tissue. The exigencies of military radiographic work also render adequate protection difficult. The author then proceeds to discuss ultra-violet radiations, and photographs are reproduced of the spectra of various arcs, viz. mercury, silver, copper, the Simpson arc, and carbon. The radiation from the Simpson arc, consisting of pole pieces of wolframite, the main constituent of which is tungsten, is very rich in ultra-violet rays. Experiments were made to show the penetrating power of the ultra-violet rays from this source, means being taken to prevent, as far as possible, direct access of the blood to the part receiving the rays. Pieces of human skin, respectively one-tenth, one-half, and 1½ mm., were placed in front of the slit of the spectrograph. It was found that skin was very absorbent for the ultra-violet radiation, and less than one part in a thousand of this radiation penetrates to a depth of half a millimetre. As the wave lengths approach the region of visible radiation the rays become rather more penetrating, but it is doubtful whether as much as 1 per cent. of the radiation penetrates to a depth as deep as 1 mm.—a small percentage, however, penetrates 1½ mm. In order to ascertain the extent to which tungsten contributes to the ultra-violet radiation from the Simpson arc two electrodes of pure tungsten were obtained, and the spectrum, photographed in the same manner, showed that the two spectra are apparently identical. S. E. D.

THE SIMPSON LIGHT: ITS NATURE, MODE OF PRODUCTION, AND APPLICATION, WITH A PRELIMINARY NOTE ON ITS THERAPEUTIC PROPERTIES. W. DOUGLAS HARMER and E. P. CUMBERBATCH. (*Lancet*, January 8th, 1916, p. 76.)

THE Simpson light is made up of rays of two kinds: (1) Visible rays—violet, blue, green, etc., down to red; (2) invisible rays—viz., heat rays and ultra-violet rays. It is to the last that the therapeutic properties of the lamp are mainly due. The light is emitted from an electric arc formed between electrodes chiefly consisting of a tungstate of iron and manganese, known as wolfram, and has claims for clinical investigation by reason of its greater richness in ultra-violet rays and the presence of rays of shorter wave-length than that emitted from electrodes of other metals employed under similar conditions. The lamp consists of adjustable electrodes mounted on a metal stand, and the light may be applied either by the "open arc" method with a plane mirror, the electrodes being placed 12 to 15 in. from the skin, which is exposed for from two to five minutes according to the reaction observed after the first exposure; or by the "focussed arc" method, a parabolic reflector being used; or by the "medium focussed arc" method, the rays being reflected to a blunter focus for the treatment of areas of medium size. The vapour produced during the burning of the lamp is also used for inhalation in the treatment of respiratory affections. The application of the light produces an erythema of short duration five or six hours after the exposure. The authors report the results obtained in a number of different diseases. They conclude that it is too early to form any opinion as to the value of the Simpson light, but believe that it will be of distinct value in the treatment of superficial ulcerations, especially those which are of a purulent character. Beyond a slight reaction, which is quite definite when a long exposure has been given, no bad results were seen.

S. E. D.

SOME EXPERIMENTS WITH THE SIMPSON ARC LAMP. Dr. J. H. SEQUEIRA. (*Lancet*, February 19th, 1916, p. 405.)

THE writer points out that the proper understanding of the use of concentrated actinic light in the treatment of disease is due to the late Professor Finsen, who showed that the penetration of living tissues could only be obtained by rendering them anæmic, and an essential part of the treatment to which his name is attached consists in compressing the parts subjected to the light. It is the ignoring of this fact which demands close examination of the contentions urged by the exponents of the Simpson lamp. Several lamps giving off a high proportion of actinic rays have been used since the early days of phototherapy, although these have not ousted the Finsen lamp in the treatment of lupus. It would be remarkable if a light rich in actinic rays, such as that of the Simpson lamp, failed to benefit certain superficial bacterial ulcerations, but the author's experiments prove conclusively that the penetrative power of the light is negligible and that the radiations have nothing in common with the X-rays. The experiments were made with paper, dental films, aluminium, gutta-percha tissue, frog's skin, and fresh human skin placed on the author's arm, which was then exposed to the light. The result was that the rays failed to penetrate any of these tissues, while an acute erythema was set up in the uncovered skin. In similar experiments a piece of glass stopped the rays while rock-crystal allowed them to pass. A piece of sensitised paper placed behind the lobule of a patient's ear was also unaffected.

The author concludes: (1) That the rays given off by the Simpson arc are actinic rays. There is no essential difference between them and actinic rays derived from other sources of light. (2) That like other actinic rays they have no penetrative power. They will not pass through fresh human skin, frog's skin, paper, cotton, or gutta-percha tissue. (3) That they are not X-rays and have nothing in common with X-rays. (4) That any deep effects which have been observed are due to counter-irritation, and are similar to those produced by the application of a mustard plaster or those seen from the use of light baths.

S. E. D.

SYPHILIS.

THE PATHOLOGY OF SYPHILIS. By J. A. Fordyce, M.D. (*Journ. Cut. Dis.*, 1915, xxxiii, p. 802.)

In this paper, which was read before the thirty-ninth annual meeting of the American Dermatological Association in New York in 1915, a general survey is given of the present state of our knowledge of the pathology of syphilis, the nature of the infection, the reaction which the spirochæte calls forth in the tissues, and the pathological changes which follow. The different organs of the body are dealt with seriatim, and the paper is illustrated by a series of excellent photo-micrographs. J. M. H. M.

A STUDY OF THE COMPARATIVE TOXICITY OF THE VARIOUS PREPARATIONS OF MERCURY. By J. F. Schamberg, M.D., J. A. Kolmer, M.D., G. W. Raiziss, Ph.D. (*Journ. Cut. Dis.*, 1915, xxxiii, p. 819.)

The most efficacious results from the use of mercury in syphilis are obtained from the employment of massive doses; hence it is highly important that an accurate knowledge should exist of the comparative toxicity of the various preparations in use. A rapid method of testing the toxicity of the different salts is by determining the immediate lethal dose. For this purpose solutions of various salts were injected into the veins of rabbits, repeated injections being administered at intervals of one or two minutes until death ensued. By this means it was discovered that the succinimide of mercury was the most toxic salt as far as immediate lethal effect was concerned, 3½ milligrammes per kilo of bodyweight proving fatal. Following this in order of toxicity came the oxycyanide, the bichloride, benzoate, cacodylate, sozoiodolate, and finally the salicylate, the last being rendered soluble in piperazin water. The cacodylate can be given in larger amount than any of the above salts.

An endeavour was then made to determine the maximum dose which could be given without inducing a fatal result (dosis tolerata). The doses were given both intramuscularly and intravenously, and it was found that four times more mercury could be borne by intramuscular administration than by intravenous infusion.

A comparison of the toxicity of the insoluble mercurial preparations was also made—namely, of calomel, grey oil, and the salicylate of mercury.

A large proportion of the experimental animals succumbed to mercurial intoxication, were autopsied, and histological examinations were made of the various organs, particularly the kidneys. It was found that even in animals receiving small and non-fatal doses of mercury, but autopsied after an interval of six or seven weeks, that well-defined changes were apparent in the tubules, the result of direct degeneration of the cells.

The conclusions arrived at by the writers were as follows:

The maximum tolerated dose of the various salts of mercury may be widely divergent, but, when the doses are calculated in terms of pure mercury, they fall within relatively narrow limits, the toxicity of the various salts being directly proportionate to the amount of pure mercury contained.

The inorganic salts, as represented by the bichloride of mercury, were found to be no more toxic than the numerous organic combinations which are commonly employed. The bichloride of mercury was fatal, on the average, in intravenous doses above 2 milligrammes per kilo of bodyweight. Administered intramuscularly, it was fatal above 6 milligrammes per kilo of bodyweight.

The insoluble preparations, such as grey oil, calomel, and the salicylate, were absorbed at the rate of a little over 1 per cent. of the injected amount per day, and even at the end of six weeks almost 50 per cent. of the mercury of insoluble preparations might be unabsorbed at the site of injection; hence the injection of the usual doses of the insoluble compounds at weekly intervals must lead to an accumulation of the drug in the tissues.

Mercury had a great affinity for the cells of the kidney, and this organ was one of the earliest involved in mercurial intoxication. Hence during the intensive treatment with mercury, the necessity of careful examination of the urine from time to time should be emphasised. The nephritis produced by mercury was primarily tubular in variety; capsular glomerulo-nephritis of the exudative (hæmorrhagic) variety was frequent, and practically always accompanies severe tubular nephritis. Calcification of the degenerated tubular cells was found within forty-eight hours after the administration of mercury, and always occurred in severe mercury nephritis, irrespective of the salt administered or the route of injection. J. M. H. M.

SALVARSAN IN PRIMARY SYPHILIS: FIVE YEARS' EXPERIENCE WITH "606." A. A. Uhle and W. H. Mackinney. (*New York Med. Journ.*, January 1st, 1916, p. 6.)

The writers comment upon the results of salvarsan and neosalvarsan in fifty-seven patients with genital or extra-genital chancres treated since 1910. They conclude that—(1) The earliest positive diagnosis of syphilis depends upon the demonstration of *Treponema pallidum* in the expressed serum of a suspected sore. (2) This examination is best made with the dark field illumination microscope. (3) The Wassermann reaction is of value in the diagnosis, as a positive reaction means the onset of systemic syphilis, while a negative reaction for practical purposes means a local infection only. (4) Experience shows that when energetic salvarsan or neosalvarsan treatment is introduced before the advent of a positive Wassermann reaction a radical cure is the rule. (5) After the Wassermann reaction is once positive such uniformly good results cannot be expected. (6) When possible, excision of the chancre is a valuable addition to treatment. S. E. D.

A CASE OF DEATH FOLLOWING AN INTRAVENOUS INJECTION OF GALYL. H Hastings Willis. (*Med. Journ. of Australia*, December 4th, 1915, p. 536.)

The patient was a single man, aged 30 years, who applied for treatment on August 30th, 1915, for a primary sore on the penis of ten days' duration. On September 8th a diagnosis of generalised syphilis was made, as the glands at the posterior border of the sterno-mastoid muscles were enlarged and hard. One mercurial injection (half a grain) was given.

On September 15th he received an intravenous injection of galyl (equivalent to 0·9 grm. neo-salvarsan) without misadventure.

A week later (September 22nd) he was given a similar dose in the usual way.

The operation was performed easily, and the patient appeared quite well, and got up off the couch holding a pad of cotton wool over the site of injection. Three minutes afterwards he said he was faint, and staggered. He was assisted on to a couch, and said he felt tingling sensations all over him. His respiration was normal. About two minutes later he got up, walked across the room, and vomited. He broke out in a profuse perspiration, and would not reply to questions, though he appeared to understand what was said to him. He was seated in a chair when, quite unexpectedly, he fell on to the floor, became unconscious, and passed urine involuntarily, while his pulse became feeble and intermittent and his breathing irregular and stertorous. He was then admitted to the emergency ward.

On examination there, at 8.30 p.m., he was still unconscious, his pupils were equal and small, his eyes not deviated. Both the light reflex and the corneal reflex were absent on the right side, but present on the left. His muscles were completely relaxed. Breathing was shallow and Cheyne-Stokes in character, and his pulse 64, regular, and of good volume and tension. His colour was good, and his temperature 97·6° F. He was bathed in a profuse cold perspiration.

At 9.5 p.m. he had a convulsion, in which his respiration became stertorous, the cheeks being blown out with each expiration. He became rigid in all his limbs, but no definite attitude was adopted. All his reflexes were exaggerated, and Babinski's sign and ankle clonus were present on both sides. His eyes were deviated strongly to the left, and all eye reflexes were present. This convulsion lasted three minutes, and after it breathing became quiet and shallow, but the deviation of the eyes and the increased reflexes and double Babinski's sign remained until the end.

At 9.15 p.m. he had a second convulsion with stertorous breathing lasting seven minutes, and at 11.30 p.m. he had another convulsion lasting three minutes.

At 2.45 a.m. the temperature was 108·4° F., pulse 160 and feeble, but the nervous signs were unchanged.

Death occurred about 8.30 a.m.

A post-mortem examination was made twenty-five hours after death. The brain showed no abnormality, and on sectioning after hardening in formalin no hæmorrhage was found. The pleuræ each contained about 10 oz. of blood-stained fluid, and both lungs showed great venous congestion. The pericardium contained 2 oz. of blood-stained fluid. In the small intestine a bright red coloration about 4 ft. from the ileo-cæcal valve, over an area of about 9 in., was noted. The spleen and kidneys were congested. There were venous engorgement and fatty changes of the liver. No arsenic was found in the liver, stomach, and intestines.

That the fatal injection was the second suggests to the author the probability that the phenomena were anaphylactic in nature. J. H. S.

ON THE BACTERICIDAL POWER ACQUIRED BY THE SERUM AFTER THE ADMINISTRATION OF SALVARSAN OR NEOSALVARSAN. S. R. Douglas and L. Colebrook. (*Lancet*, January 22nd, 1916, p. 181.)

The authors summarise their conclusions as follows:

(1) Neosalvarsan and salvarsan in watery solutions possess a very distinct

bactericidal power against staphylococcus when the strength of the solution is 1 in 6000. When the solvent largely consists of blood or serum this power is slightly diminished. The bactericidal power of both these preparations appears to be practically the same.

(2) The administration of neosalvarsan in ordinary doses renders the blood fluids markedly bactericidal. This power lasts but a short time, and seems to reach its maximum about one hour after the administration of the drug, diminishing rapidly in the third and fourth hours.

(3) Heating the serum to 60° C. for from ten to twenty minutes has no deleterious effect on this bactericidal power, showing that it is not in any way due to the development of immune bodies in the serum, and this fact, together with the short period in which the serum is found to be bactericidal, strongly suggests that the bactericidal power is due to some arsenic compound in solution in the blood serum.

(4) Salvarsan which, as mentioned above, has almost identically the same bactericidal power as neosalvarsan in *in vitro* experiments gave practically no demonstrable bactericidal power to the patient's serum when ordinary therapeutic doses were administered, but it was constantly noticed that organisms which had been treated with serum obtained within three hours of the administration of the drug grew very much more slowly than normally and were agglutinated into masses.

(5) In view of the very distinct bactericidal power which the serum acquires after the administration of neosalvarsan, it is reasonable to hope that the administration of this drug, or some similar preparation, such as neokharsivan, would have a beneficial effect on wound or other similar septicæmias and might even strikingly assist in the sterilisation of deep and irregular suppurating wounds. S. E. D.

CORRECTION.

"Pemphigoid Eruptions following Vaccination." By Dr. W. H. Mook. The Editor regrets that in the abstract of this paper which was printed in the number for November, 1915, Dr. Mook's name appeared wrongly as Dr. Moore.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

ERYTHEMAS, INFLAMMATIONS, ETC.

Anthrax, Infection by a Shaving Brush, A Fatal Case of. E. H. SNELL. With Clinical Notes by E. W. G. MASTERMAN. (*Lancet*, January 29th, 1916, p. 242.)

Anthrax conveyed by Infected Shaving Brushes, An Outbreak of. R. R. ELWORTHY. (*Lancet*, January 1st, 1916, p. 20.)

Anthrax. A Fatal Case of Infection by a Shaving Brush. H. L. TIDY. (*Lancet*, January 29th, 1916, vol. cxc, p. 242.)

Bullous Diseases. J. M. H. MACLEOD. (*The Practitioner*, December, 1915, vol. xcv, p. 788.)

Disseminated Miliary Tuberculosis, General, X-ray of the Lungs and Illustrations of Skin Lesions. W. P. NORTHRUP. (*Arch. of Ped.*, December, 1915, vol. xxxii, p. 887.)

Elephantiasis in a Child aged 12 years. C. S. DE LO TERREROS. (*La. Med. de los Niños*, 1915, vol. xvi, p. 105.) (Abstr. *Brit. Journ. of Child. Dis.*, 1916, vol. xiii, p. 57).

Erythema Vasculosum. On a hitherto undescribed Dermatosis. B. LIPSCHÜTZ (Przemysl). (*Wien. klin. Wochenschr.*, October 7th, 1915, vol. xxviii, No. 4, p. 1073.)

Exanthem with Epidemic Meningitis. H. MORGENSTERN. (*Deutsch. Med. Wochensch.*, November 11th, 1915, vol. xli, p. 1363.)

Granulosis Rubra Nasi and Tuberculosis. GOUGEROT. (*Bull. de la Soc. Fran. de Derm. et de Syph.*, (July 2nd, 1914), No. 7, 1915, p. 344.)

Hemiatropia Sclerotica of the Left Side of the Face in the Region of the Third Branch of the Fifth Nerve, With Incipient Diffusion to the Territory of the First and Second Brachial. G. VERROTTI. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1915, vol. lvi, p. 413).

Herpes in Pneumonia and Pneumococcal Infection, On the Significance of. J. PERROT. (*Thèse de Lyon*, 1913–14. No. 130.) (Abstr. *Brit. Journ. of Child. Dis.*, 1916, xiii, 58.)

Herpes in Diphtheria, The Occurrence of Diphtheria Bacilli in the Vesicles of. RALL. (*Münch. med. Wochenschr.*, 1915, lxii, p. 396.) (Abstr. *Brit. Journ. of Child. Dis.*, 1916, xiii, 59.)

Herpes Zoster of Unusual Distribution (Bilateral). GORDON WARD. (*Lancet*, December 4th, 1915, clxxxix, p. 1272.)

Hyperkeratosis Lacunaris. E. URBANSCHILSCH. (*Mediz. Klin., Berl.*, November 7th, 1915, xi, No. 45, p. 1228.)

Itching, Origin and Cure of. P. G. UNNA. (*Berl. Klin. Wochenschr.*, November 29th, 1915, lii, Nos. 42–48.)

Lupus Follicularis Disseminatus. G. NOBL. (*Derm. Wochenschr.*, December 18th, 1915, Bd. lxi, No. 51, p. 1163.)

Pellagra, Symposium on. Southern Medical Association, Ninth Annual Meeting, Dallas, Texas. (*Journ. Amer. Med. Assoc.*, December 4th, 11th, 11th, 1915, vol. lxv, pp. 2029, 2114, 2195.)

Pellagra, On the Ætiology of. N. LATRONICO. (*Gazz. d. Ospedali e d. Clin.*, December 5th, 1915, No. 86, p. 1345.)

Pityriasis Lichenoides (better Polymorpha) Chronica, which combines the Three Types of Parapsoriasis, Remarks on the Work of Prof. Werther on a Case of. MAX LEIBKIND. (*Derm. Zeitschr.*, November, 1915, Bd. xxii, Heft 6, p. 671.)

Pyodermatoses of the Lower Extremity in War, The Treatment of. M. STRAUSS. (*Deutsch. med. Wochenschr.*, December 23rd, 1915, vol. xli, No. 52, p. 1551.)

Pyogenic Dermatoses, Bacterin Treatment of. (*Boston Med. und Surg. Journ.*, December 16th, 1915, vol. clxxiii, No. 25.)

Purpura Hæmorrhagica, Intra-muscular Injections of Whole Blood in the Treatment of. (*Journ. Amer. Med. Assoc.*, January 1st, 1916, vol. lxvi, p. 20.)

Quincke's Œdema, On the Pathogenesis of. Paul Neuda. (*Wien. klin. Wochenschr.*, December 22nd, 1915, vol. xxviii, No. 51, p. 1407.)

Symmetrical Spontaneous Gangrene of the Extremities (Raynaud's Disease). (G. de Gaetani Quinta. (*Gazz. d. Ospedali e d. Clin.*, November 21st, 1915, No. 82, p. 1281.)

Tender Feet and Verruca Plantaris. Annotation. (*Lancet*, January 22nd, 1916, vol. cxc, p. 199.)

Zona followed by a Generalised Eruption of Aberrant Vesicles, Cytology. E. Jeanselme and A. Touraine. (*Bull. de la Soc. Fran. de Derm. et de Syph.* (July 2nd, 1914), No. 7, 1915, p. 351.)

Zona, The Diagnosis and Therapy of. Franceschini. (*Gazz. d. Ospedali e d. Clin.*, December 2nd, 1915, No. 85, p. 1344.

DERMATITIS MEDICAMENTOSA, TRAUMATICA, ETC.

Dermatitis Facticia (with Six Illustrations). H. K. Gaskill. (*New York Med. Journ.*, January 22nd, 1916, vol. ciii, p. 148.)

Dermatitis Medicamentosa, Case of. W. S. Walsh. (*Boston Med. and Surg. Journ.*, December 16th, 1915, clxxiii, No. 25.)

Industrial Skin Lesions in Workers in Munitions, with Special Relation to the Prevention of Mercurial Action. M. Oppenheim. (*Wien. klin. Wochenschr.*, November 25th, 1915, xxviii, No. 47, p. 1273.)

Pyrogallol Poisoning, The Prophylaxis of. Max Bockhart. (*Derm. Wochenschr.* September 11th, 1915, lxi, No. 37, p. 859.)

Simulation, Case of Face Ulcer in an Hysterical Woman. Hans Marx (illustrated). (*Derm. Wochenschr.*, September 16th, 1915, lxi, No. 38, p. 883.)

Traumatism and Scleroderma. Georges Thibierge. (*Ann. de Derm. et de Syph.*, December, 1915, vol. v (1914–1915), No. 12, p. 645.)

NEW GROWTHS.

Adenoma Sebaceum of Pringle, On Multiple Symmetrical Nævi, *apropos* a Case of the So-called. P. L. Bosellini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1915, lvi, p. 369.)

Anatomic Distribution of Cutaneous Neoplasms, The. F. T. van Beuren, jun. (*Journ. Amer. Med. Assoc.*, 1916, lxvi, No. 2, p. 112.)

Lymphogranulomatoses (Hodgkin's Disease) with Pemphigoid Ex- and Enanthemata in connection with Granulomatous Skin Nodules. Ehrich Hoffmann. (*Deutsch. med. Wochenschr.*, September 16th, 1915, xii, No. 38, p. 1117).

Melanotic Carcinoma of the Nail-bed. W. Dubreuith. (*Bull. de la Soc. Fran. de Derm. et de Syph.* (July 2nd, 1914), No. 7, 1915, p. 399.)

Precancerous Dermatoses: A Sixth Case of a Type Recently Described. J. T. Bowen. (*Journ. of Cut. Dis.*, December, 1915, vol. xxxiii, No. 12, p. 787.)

Sarcoma cutaneum telangiectaticum multiplex ("Akrosarkoma" Kaposi) with Joint Affection. E. Rasch. (*Derm. Zeitschr.*, October, 1915, Bd. xxii, Heft. 10, p. 575.)

DISEASES OF HAIR AND NAILS, PIGMENTATION, ETC.

Alopecia and Its Treatment. W. K. Sibley. (*The Practitioner*, December, 1915, vol. xcv, p. 807.)

Alopecia Areata Neurotica after Shell-wound. A. PÖHLMANN. (*Münch. med. Wochenschr.*, November 23rd, 1915, lxii, No. 47, p. 1623.)

Alopecia Areata. DOUGLAS FRESHWATER. (*The Practioner*, December, 1915, vol. xcv, p. 796.)

Contralateral Alopecia after Head-wound. A. V. KNACK. (*Derm. Wochenschr.*, August 21st, 1915, xli, No. 34, p. 811.)

Diffuse Pigmentation of the Skin after Shell-wound in the Vicinity of the Kidney. W. FISCHER and H. LESCHCZINER. (*Derm. Wochenschr.*, December 4th, 1915, Bd. lxi, No. 61, p. 1115.)

Family Vitiligo and Hereditary Syphilis. GOUGEROT. (*Bull. de la Soc Fran. de Derm. et de Syph.*, No. 7, July, 1914–December, 1915, p. 234 (Séance July 2nd, 1914).)

Growth of the Hair and Nails in the Course of the Repair of Wounds of War. (Hypertrichosis of Traumatic Origin.) E. GLEY and R. LOEWY. (*Compt. rend. Soc. de biol.*, 1915, lxxviii, p. 204.)

Hypertrichosis, Variations in Female Secondary Sexual Characteristics and Internal Secretions. J. R. MCAULIFF. (*Journ. Amer. Med. Assoc.*, January, 1916, lxvi, No. 1, p. 15.)

Trichokyptomania. R. L. SUTTON. (*Journ. Amer. Med. Assoc.*, January, 15th, 1916, vol. lxvi, No. 3, p. 185.)

Vitiligo Syphilitic. RALPH and GALLIOL. (*Bull. de la Soc. Fran. de Derm. et de Syph.*, July 2nd, 1914, No. 7, 1915, p. 357.)

Vitiligo and Syphilis. L. M. PAUTRIER. (*Bull. de la Soc. Fran. de Derm. et de Syph.* (July 2nd, 1914), No. 7, 1915, p. 355.)

FUNGUS INFECTIONS.

A Contribution towards the Demonstration of Pathogenic Skin Fungi. K. HERSCHEIMER. (*Derm. Zeitschr.*, November, 1915, Bd. xxii, p. 633.

Eczema Marginatum Hebræ: An Epidemic in a Hospital. W. FISCHER. (*Deutsch. med. Wochenschr.*, November 25th, 1915, xli, No. 48, p. 1422.)

Epidermomycosis Eczematoid due to Parasites of the Class of Yeasts. HUDELO and MONTLAUR. (*Bull. de la Soc. Fran. de Derm. et de Syph.* (July 2nd, 1914), No. 7, 1915, p. 403.)

Experimental Pseudoactinomycotic Formation from Achorion Schönleinii and Trichophyton Violaceum. F. RADAELI. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1915, lvi, p. 413.)

Favus of "Autoochthon" Origin in the German Empire. N. I. GOLDKRAUT. (*Derm. Wochenschr.*, November 20th, 1915, Bd. lxi, No. 47. p. 1067.)

New Fungus (Phialophora Verrucosa), A Cutaneus Lesion caused by a. C. G. LANE. (*Journ. of Cut. Dis.*, December, 1915, vol. xxxiii, No. 12. p. 840.)

Prevention and Treatment of Ringworm and Favus of the Scalp. J. E. LANE. (*Journ. Amer. Med. Assoc.*, November 13th, 1915. vol. lxv., p. 717.)

Trichophytin Reaction in the Blood-Count, The. G. MIESCHER. (*Derm. Wochenschr.*, October 30th, 1915, vol. li, No. 44, p. 1011.)

TREATMENT.

Argulan, A New Organic Mercury Preparation. V. MEUTBERGER. (*Derm. Wochenschr.*, October 2nd, 1915, vol. lxi, No. 4, p. 931.)

Erysipelas of the Face by Painting with Aqueous Solution of Methylene Blue. Treatment of. NOBÉCOURT. (*Bull. et Mém. de Soc. Med. des Hôp. de Paris.* December 2nd, 1915, Nos. 35–36, p. 1065.)

Leprosy: Preliminary Note on the Use of Gynocardates orally and subcutaneously in. SIR LEONARD ROGERS. (*Lancet,* February 5th, 1916, p. 288.)

Levurinose in Skin-Diseases, On the Employment of. VÖRNER. (*Münch. med. Wochenschr.*, No. 46, lxii, 1915, p. 1569.)

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Mercury, A Study of the Comparative Toxicity of the Various Preparations of. J. F. SCHOMBERG, J. A. KOLMER, and G. M. RAIZISS. (*Journ. of Cut. Dis.*, December, 1915, vol. xxxiii. No. 12, p. 819.)

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Subcutaneous Injection of Distilled Water for Multiple Ulcers. S. ARBOUR STEPHENS. (*Lancet,* December 18th, 1915, clxxxix, p. 1351.)

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Skin-Diseases of Childhood. I. SCHAYER. (*South Carolina Med. Assoc. Journ.* November, 1915, xi, No. 11, p. 368.)

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Histology of the Exanthem in Typhus, and an Unusual Case of Postexanthematic Skin Change. J. KYRLE and G. MORAWETZ. (*Wien. Klin. Wochenschr.*, November 25th, 1915, xxviii, No. 47, p. 1286.)

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PERSONAL NOTE.

Drs. H. H. Whitehouse and A. S. Clark have been appointed Professors of Dermatology at the New York Post-Graduate Medical School and Hospital.

DEATHS.

Prof. T. von Marschalkó, Kolozsvár.
Prof. J. C. White, Boston, U.S.A.
Prof. G. T. Jackson, New York.

ANNOUNCEMENT.

The Cambridge University Press announce that they have been appointed agents for the following two journals: The *Journal of Cancer Research* (quarterly), the official organ of the American Association for Cancer Research, and the *Journal of Immuniology* (bi-monthly), the official organ of the American Association of Immuniologists and the New York Society of Serology and Hæmatology.

The subscription price for each journal will be 23*s.* net.

THOMAS COLCOTT FOX.

THE BRITISH
JOURNAL OF DERMATOLOGY.

APRIL–JUNE, 1916.

THOMAS COLCOTT FOX.

Thomas Colcott Fox passed away on April 11th, in his 68th year. The news of the event caused deepest gloom in our world of British Dermatology, and will doubtless do the same wherever our Journal penetrates. Our Editor has asked me to write a personal appreciation of the man, as he has deputed Dr. Adamson to sum up his work. The task is as easy as it is sad, for I saw much of Colcott Fox during the last thirty-five years of his life—which was an open book—and I enjoyed during that time the privilege of intimate personal friendship with him.

Colcott Fox's training and temperament were those of a typical English gentleman. He was a son of Dr. L. O. Fox, of Broughton, Hants, and to the end of his life he passionately loved his quiet country home, its highways and hedges, its people, its manners, and its pursuits. He was educated at University College School, and early evinced his scientific bent of mind by gaining a Scholarship in Natural Science at Peterhouse College, Cambridge. He played cricket for his College and for his County; he was an enthusiastic and good all-round sportsman; he skated admirably and was a more than average golfer. Whatever he took up he did well, and in doing so he made himself popular all along the line.

He took his M.R.C.S., and graduated as M.B.London in 1876; he became a Member of the Royal College of Physicians in 1883, and was elected to the Fellowship in 1892. His first public Medical appointment was that of Superintendent of the Fulham Smallpox Hospital. The meteoric success of his talented elder brother, Tilbury, attracted him irresistibly towards Dermatology, and he was early in his career appointed Physican to the Department for Diseases of the Skin at Westminster Hospital, a post he held with *éclat* till the end of his professional life. Although his clinic was—at least for many years—a comparatively small one, it was characteristic of the loyalty and fidelity of the man that he could never be persuaded to resign it for any more brilliant post; and it must be regarded as redounding to his credit that his abundant and admirable work was the result of thorough and exhaustive study of a comparatively small amount of clinical material. But he possessed to a remarkable degree that "capacity for taking pains" which almost amounts to genius.

Colcott Fox's name will, however, chiefly be handed down to posterity as a master-teacher who attracted, guided, and helped all who came within the sphere of his almost magnetic influence. By his pupils—and they were many—as by his patients he was adored. And no man ever made less effort to gain popularity, or was more spontaneously natural in manner and speech. He had in reality the heart of a child; he knew neither envy, malice, nor uncharitableness. Intensely as he detested "crookedness," presumption, humbug, and insincerity—personal or professional—his attitude towards others who exhibited these qualities was always one of pitying contempt.

Duty was his watchword, generosity his guiding motive in life. He gave of his best freely and to all without thought of emolument or recompense. He has the reward he would value most enshrined in the affectionate remembrance of many sincere friends in many countries.

The last three years of his life—owing to failing health—were passed in comparative seclusion, guarded and tended solicitously by his devoted wife. Calmly, intrepidly, unfalteringly, unmurmuringly, he trod the dark valley of the shadow, and he passed away with a smile on his lips. His mortal remains lie buried beneath the waving greenery of the trees he loved so well in the beautiful little churchyard of the parish of Holt Cross, in Worcestershire. *Requiescat!*

J. J. PRINGLE.

THE WORK OF THOMAS COLCOTT FOX.

Two features particularly characterised the dermatological work of the late Dr. T. Colcott Fox: his profound knowledge of the literature of diseases of the skin, and his own very accurate clinical observation. It is probable that no dermatologist had a wider knowledge of the literature of skin-diseases. The monographs which he collected during many years, and which are now in the Library of the Royal Society of Medicine, are evidence of his indefatigable industry. His reading ranged from the earlier masters, from Willan and Bateman and from Bazin, to the latest pamphlets in the dermatological journals of to-day. It is possible that his accurate knowledge of what others had observed and noted withheld him from writing what had already been recorded, and accounted in some degreee for the restraint with which he himself wrote upon dermatological subjects. For, although he contributed largely to the advance of our knowledge of skin-diseases, he was no prolific writer, and for the most part his papers were brief, though careful and to the point. His knowledge of the writings of old masters of dermatology, combined with his own accurate observation, enabled him to revive our interest in many now well-known skin-diseases which had been earlier described and forgotten.

That which Dr. Fox wrote was addressed to the dermatologist rather than to a large medical public, so that a record of his writings would seem to find here an appropriate place, and will, it is believed, be of interest to the readers of this Journal.

The work of Dr. Colcott Fox, as a dermatologist, covers a period of nearly forty years. Soon after obtaining a qualification, in 1876, he began as assistant to his brother Tilbury, who was in charge of the Skin-department at University College Hospital, and his name appears, in 1876, with that of Tilbury Fox as part author of the third edition of *The Epitome of Skin Diseases.*

During the next few years he contributed to the weekly medical journals and to the Transactions of the Medical Societies papers on Trichorrexis nodosa (1878), Purpura from Iodide of Potassium (1879), Morphia eruption (1879), Xanthelasma multiplex (1879), Histology of Molluscum contagiosum (1879), Rodent ulcer (1879), Lymphangiectodes (1879), The Neurotic Origin of Lichen planus (1880), Erythema gyratum (1880), Herpes iris of Bateman (1881), Chromidrosis (1881), Urticaria pigmentosa (1883). His description of Lymphangiectodes was the earliest account of this disease, while a note on two cases of Erythema gyratum perstans in the Clinical Society's Transactions (1881) stands as a record of a hitherto undescribed persistent ringed erythema, which must be credited to Fox as one of the several diseases to which he first drew attention.

In 1880 he edited a posthumous paper of Tilbury Fox on "A Clinical Study of Hydroa," which he summarised again in 1911 in his own article on the Pemphigoids in Clifford Allbutt and Rolleston's *System of Medicine*. He regarded his brother's paper as the prototype of Duhring's writings on Dermatitis herpetiformis, which appeared in 1884 and onwards, and he felt always that Tilbury Fox's work as a pioneer in this direction was never sufficiently recognised.

The subject of drug eruptions was also one to which Colcott Fox returned in later years, when he edited with notes for the New Sydenham Society, Prince Morrow's well-known monograph on drug eruptions.

The reports of a case of "Feigned Skin-eruption" and two cases of "So-called Erythema gangrænosum" were contributions towards our knowledge of the self-inflicted skin lesions in hysterical girls and in malingerers to which Wilson, Sangster, and Liveing had already called attention, and which almost to this day German writers have continued to regard as neurotrophic gangrenous manifestations. To these eruptions Fox, who proved in several instances that they were self-inflicted, was accustomed to apply the term Dermatitis ficta, and he gave a very full account of the literature of this subject in a paper in the *Illustrated Medical News* in 1889.

In 1884 he wrote in the *Lancet* a short paper on the now well-known disease of the skin, Pityriasis maculata et circinata, which had not previously been described in this country, and to which his attention had been called by the exhibition of Duhring's case in America in 1880. In this paper he established the claim of Gibert to be the first to describe this eruption, which we now call Pityriasis rosea of Gibert.

From 1884–1887 Dr. Fox contributed an annual survey of the work of the Skin-department to the Westminster Hospital Reports, and among the cases of special interest which he recorded in these characteristically careful records were "A Case of Macular Atrophy Three Years after a Secondary Syphilitic Eruption," his earlier cases of Pityriasis rosea, and the first case of Acne scrofulosorum published in this country.

In 1888 Colcott Fox became Editor, with Bruce Clarke, of a weekly journal, *The Illustrated Medical News*, which ran into six bi-annual volumes. To this journal Fox contributed admirable articles on infantile scurvy, and notes on multiple fracture and softening of the bones in infants, which remind us that he was at one time Physician to the Victoria Hospital for Children. He also contributed the lecture, to which reference has already been made, on "Feigned Eruptions," and a record of some cases of Lymphangiectosis of the hands and feet in children, which has since been recognised as the earliest account of the disease we now know as Angiokeratoma of Mibelli and Pringle. Other contributions were "Xeroderma pigmentosa" and "A Case of Erythema iris."

We may now return to the year 1882, in which there occurred an event of much importance for dermatology in this country, namely, the founding of the Dermatological Society, a society which has continued its course to the present day, merging in 1907 as a tributary with the greater stream of the Royal Society of Medicine.

Although the official publication of the Proceedings of the Society did not begin until 1894, we are fortunate in possessing, from the pen of Dr. Fox, a record of its inception and notes of the cases shown during the whole of the years from 1882 to 1894. These private notes were published at the request of many of Dr. Fox's dermatological colleagues in the *British Journal of Dermatology* in 1907, and, in Fox's own words, "although admittedly imperfect, will serve to show the wealth of clinical material exhibited during that period, and cannot fail to be both of practical and historical value to all interested in cutaneous medicine and its development in this country."

Dr. Fox there tells us that the Society was one of the first which was established exclusively for the study of skin-diseases, and that its inception was due to the late Dr. Alfred Sangster and to Dr. J. H. Stowers, who became its first secretaries.

The names of the twenty-three original members are all well known as contributors to our knowledge of skin-diseases; among them were Erasmus Wilson, John Cavafy, Stephen Mackenzie, George Thin, Morrant Baker, Colcott Fox, Radcliffe Crocker, Dyce Duckworth, Jonathan Hutchinson, Robert Liveing, Malcolm Morris, J. T. Payne, P. H. Pye-Smith, Frederick Taylor, Alfred Sangster, and J. H. Stowers. Two of these names still adorn our present list of members; one other, that of J. J. Pringle, was added two years later, and

Pringle and Fox became Hon. Secretaries, and remained so for the next fifteen years.

Among the more noteworthy achievements of the old Dermatological Society was the establishment of the identity of the eruptions we now call Tuberculides. As is well known, Colcott Fox helped very largely to introduce a knowledge of these important affections into this country, and his interest in them was no doubt stimulated by the discussions on cases exhibited at the meetings of the Society. The first examples of the acneiform group of tuberculides to be noted in this country were exhibited by Fox in 1883 and 1885, and some of his earlier cases were reported in the Westminster Hospital Reports in 1888. Fox at this time recognised his cases as examples of the affection which Bazin had long before called Acne scrofulosa. During the next ten years other cases were exhibited by Pringle and by Stowers, and four more cases by Fox, and then a paper on the subject was read by Crocker at the International Congress in Vienna. Fox's well-known paper on Acne scrofulosorum in infants appeared in 1895.

Cases of Erythema induratum scrofulosorum of Bazin were also exhibited at these earlier meetings, first by Pringle and then by others, and Fox published an account of the disease in the *British Journal of Dermatology*. Of this paper, Dr. Pringle has written: "In 1893 Dr. Colcott Fox, in a characteristically thorough and illuminating paper, described for the first time in this country the Erythema induratum of Bazin, a condition now familiar to the merest tyro."

Another now familiar affection which owes its discovery to a somewhat later period of the Dermatological Society is Granuloma annulare, and to Fox again is due the credit of having observed and noted the earliest cases on record. In 1895 and 1896 he exhibited two cases of a "ringed eruption," afterwards described independently by Dubreuilh and subsequently named Lichen annularis by Galloway and Granuloma annulare by Crocker in 1902.

Fox, too, first observed the mild forms of Hydroa æstivale which we now recognise as types intermediate between Hutchinson's Summer prurigo and Bazin's more severe Hydroa vacciniforme. Fox's cases were exhibited in 1894, 1897, 1898, and in 1899, and in 1899 and 1900 Crocker wrote about this affection under the title of "Recurrent Summer Eruption."

At a meeting of the Society on March 14th, 1883, Fox showed a case of thickly disseminated comedones on the forehead of a boy, aged 7½ years, and in 1888 published the first full account of this complaint, to which Crocker in 1884 had given the name of "grouped comedones."

Colcott Fox, as Physician for Diseases of the Skin at Paddington Green Children's Hospital—the first children's hospital in this country to have a special department for skin-diseases—was one of the earliest observers to pay particular attention to diseases of the skin in children, and infantile eczema, vaccination rashes, impetigo, ringworm, and Lichen urticatus were with him favourite topics.

Lichen urticatus—which he liked to call "Lichen urticatus of Bateman"—was another affection whose manifold features he helped to define and to make familiar to us. He showed the correctness of Thomas Bateman's contention that "the primary lesion, which usually developed at night, was not a papule, but a congestive macule . . . which rapidly disappeared and left the more durable papules which, in the daytime, dominated the scene." He described the vesicating forms, so often mistaken for varicella, and showed that Hutchinson's varicella-prurigo was a vesicating Lichen urticatus.

His papers on "Urticaria in Infancy and Childhood," and "Lichen planus in Infants" (afterwards acknowledged to be Lichen urticatus) were published in this Journal in 1890, 1891 and 1899.

Of Impetigo and Ringworm he had an enormous clinical experience, and he was naturally greatly impressed by Sabouraud's masterly work on both these subjects, and expounded with enthusiasm to his pupils Sabouraud's important distinction between the large group of streptococcal vesical or bullous Impetigoes and the follicular pustular staphylococcal eruptions. To the list of streptococcal eruptions he added his "Vacciniform ecthyma," and in Allbutt and Rolleston's *System of Medicine* he wrote a comprehensive monograph upon streptococcal and staphylococcal eruptions.

As is well known, Fox, working in conjunction with Bloxall, repeated and controlled much of the work of Sabouraud on the biology of Ringworm and he himself on the clinical and morphological side added to our knowledge in this respect. He described a primrose-coloured culture, which Sabouraud named Trichophyton sulphureum (Colcott Fox, 1908). His most noteworthy contributions to the literature of Ringworm are his papers on "The Plurality of the Ringworm Fungi" (*Brit. Journ. Derm.*, 1896, p. 241, and *Path. Soc. Trans.*, London, 1897, vol. xlviii, p. 301), and "A Further Contribution to the Study of the Endothrix Trichophyton Flora in London, Illustrated by a Collection of Cultures and Photographs" (*Brit. Jour. Derm.*, September, 1909).

A paper on a "Small Epidemic of Alopecia areata" (1913) was his last contribution to dermatology.

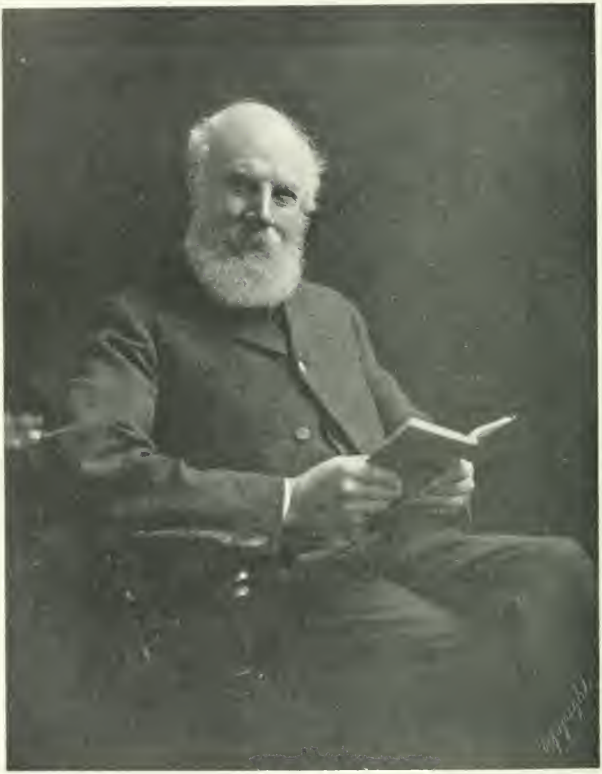
For ten years, from 1892–1901, Colcott Fox summarised the dermatological literature of the year in the *Medical Annual*, and a few years before he retired he wrote in Clifford Allbutt and Rolleston's *System of Medicine*, 1911, the following articles, each of them a monograph embodying the literature and his own particular views and observations on the several subjects dealt with: Dermatitis of Streptococcic Origin and of Staphylococcic Origin; Pityriasis; Botryomycosis; Urticaria; Angioneurotic oedema; Urticaria pigmentosa; Lichen urticatus (Bateman); The Erythemas; Erythema elevatum diutinum; Granuloma annulare; Prurigo; Schamberg's disease; Pemphigus; The Pemphigoids; Epidermolysis bullosa; Mycosis fungoides; Acne; and Seborrhoea.

H. G. Adamson.

At a meeting of the Section of Dermatology of the Royal Society of Medicine held on April 13th, 1916, the President, Dr. J. H. Stowers, referring to the death of Dr. Colcott Fox, said: "Gentlemen,—It is my melancholy duty to inform you that, after prolonged illness, and I trust but limited suffering, our old and valued friend, a former President of this Section, Thomas Colcott Fox, has passed away.

"So well known as he was to us, it will suffice on this occasion if I express from the Chair, on your behalf and mine, the deep sense of regret we all feel by the loss of one who not only held high and honourable place in the profession, and especially in the department of Dermatology, but whose character and attainments had endeared him to us for so many years.

"A fuller appreciation of his numerous qualities will be afforded us in due course, but it is well that we should be reminded to-day of the valuable work he did in our midst, of the numerous contributions



Lafayette, Glasgow.

WILLIAM ALLAN JAMIESON.

e made to our knowledge of cutaneous disease, and the personal example he set us in the honesty and uprightness of his conduct.

"The essential purposes of the life-work of Colcott Fox will long be remembered and venerated by his numerous friends and followers."

WILLIAM ALLAN JAMIESON.

ALLAN JAMIESON passed away on April 21st after some months of illness, borne with quiet resignation, at the ripe age of 77.

It will be news to most of his dermatological colleagues that he began life on a sheep run in Queensland, where he went to seek his fortune at the age of 19.

The life was not congenial to him, and after two years of it he sought and obtained his father's consent to come home and study medicine. He graduated in 1865 as the first man of the year, but, instead of following the usual custom and taking office as a Resident in the Royal, he went as assistant to a relative in general practice in Preston, where he spent two years.

In 1867 he bought a practice at Berwick-on-Tweed, where he remained for nine years, and there he laid the foundations of his friendship with the Maclagan family, which had so much influence on his career.

In 1876 he came to Edinburgh, and put up his plate in Rutland Street immediately opposite the house of Dr. John Brown of *Rab and his Friends*.

Though he had up to this period been engaged in general practice and started in that capacity in Edinburgh, he had always had a bent towards dermatology. As a student he had sat under Hughes Bennett, and watched with interest and amusement the very violent changes in treatment which occurred when Bennett took over the skin wards from Laycock and *vice versâ*, but after Bennett's death these wards were devoted to other purposes, and dermatology waned until Douglas Maclagan, who was a physician to the Infirmary in virtue of his tenure of the Chair of Medical Jurisprudence, but who had previously been one of the Ordinary Surgeons, took it up.

It was at Maclagan's instigation that Jamieson decided to qualify himself to take on the task of teaching dermatology in Edinburgh, and, taking his courage in both hands, he closed down his practice, and went to Vienna to study under Hebra.

On his return he again took up his general practice; Edinburgh was not ripe for a dermatological specialist, and he had a long fight for recognition. The older physicians almost without exception blocked all his applications, and all he could obtain at first was the post of Ordinary Physician to the Royal Public Dispensary with an extra hour for skin cases.

His next appointment was that of Consulting and Visiting Physician to the City Fever Hospital, and this he owed to the wisdom of Sir Henry Littlejohn, in whose all-powerful hands the appointment lay. Had it not been that he contracted enteric and had to resign the appointment, dermatology and fevers might have been bound together in Edinburgh as they are in one or two other medical centres.

Time and again he knocked at the doors of the Infirmary, but the opposition was always too strong until he had the good fortune to cure —with Unna's zinc gelatine—an obstinate dermatitis of the legs of a very influential medical manager. Confronted with this personal argument the opposition collapsed, and in 1884 Jamieson was appointed Extra-Ordinary Physician for Diseases of the Skin, with all sorts of reservations. It took a year or two for the students to find out that there was something to be learned from Jamieson on Saturday mornings in the little dark room which was at first allotted to him, but once they discovered him they soon crowded out the room, and compelled the migration to the West Medical Theatre, where undoubtedly he did his best teaching work.

There, Saturday after Saturday, he taught for over twenty years, and, large though the theatre is, it was often not large enough to contain the students who wished to attend. To those accustomed to teach ten or twelve students seated around them it seemed absurd to teach dermatology in this way, but Jamieson did it, and did it well. He took the cases just as they came, and, while not neglecting the general aspect, dwelt chiefly on the diagnosis and the treatment of the case in hand. Treatment was his strong point: he preached unceasingly the merits of the starch poultice and the unwisdom of strong antiseptics.

In the critical summaries of dermatological literature which he wrote for the *Edinburgh Medical Journal* may be traced the whole history of the development of modern methods. His first summary appeared in December, 1878, and dealt with the use of vaseline in skin diseases, oleate of zinc, and the inoculability of Impetigo contagiosa and Ecthyma. He wrote the last on his death-bed, and it appeared after his death.

He contributed over a hundred papers to various medical journals dealing with the whole field of dermatology, though he was perhaps most interested in the bullous affections of the skin. He had the good fortune to be the first to draw attention to the curative effects of X-rays in Mycosis fungoides.

His *Manual of Diseases of the Skin* was first published in 1888, and so successful was it that a second edition was required in the following year. The third edition appeared in 1891, and the fourth in 1894. It follows rather the lines of his famous cliniques, and the description of individual cases forms a prominent feature. They are admirably done, and no expert can read them without benefit. But other works seemed to appeal more to the practitioner and student of the more hustling times of to-day, and though he had devoted a good deal of time to the preparation of another edition, the opportunity never came.

He was devoted to his work, and after his retirement from the active staff of the Infirmary he attended regularly once a week to see the more unusual and interesting cases, and to offer suggestions for their treatment.

He had three relaxations, the study of Greek and the Greeks, archery, and cycling. He was an enthusiastic member of the Hellenic Society, and often visited Greece during the vacations. He was one of the best Archers of the King's Body Guard for Scotland, and on two occasions won the Queen's prize. Cycling he took to late in life, and he kept it up till a few months before his death.

He was elected President of the Royal College of Physicians in 1909, and held the office for two years, and he was President of the Dermatological Section at the annual meetings of the British Medical Association in 1893 and 1898. He was a Knight of Grace of the Order of St. John of Jerusalem, was Surgeon to the King's Body Guard for Scotland (the Royal Archers), and wore the Royal Household (1897) and Coronation (1911) medals.

He was a most loyal and generous colleague, and a very lovable man.

N. W.

ON SPRAYS AND SPRAYING IN THE TREATMENT OF CERTAIN SURFACE AFFECTIONS OF THE SKIN.

By W. ALLAN JAMIESON, M.D., LL.D., F.R.C.P.E.,*
Knight of Grace of the Order of St. John of Jerusalem.

The spray, which has firmly established itself as a remedy in morbid states of the larynx and nasopharynx, has been rather neglected when employed as a means of treatment in some affections of the skin. No doubt its usefulness is a restricted one, but it is of great value when suitably employed. Spirituous and oily media are available in its use. It has two great advantages, one of economy and another that it can be directed exactly on the part where it is required. But in the nature of things its action is superficial, and it is only in cases where the epidermic layers alone are disturbed that it can be employed with efficiency.

Its main field of employment is constituted by the hairy parts, which have hitherto been submitted to treatment by sprinkling on lotions or rubbing in soft ointments.

It is therefore in the slighter varieties of seborrhœic dermatitis or in the variety of disturbance of the surface of the scalp known as dandruff, in which showers of white particles are dislodged in combing or brushing the hair, that the spray finds its greatest use.

The spray itself is the ordinary hand one, provided with india-rubber bulb and atomiser. If possible it is best used by another person, who can see exactly where the cloud should be directed. Then it does not matter much how the bulb is placed in relation to the rest of the apparatus, but if the patient must use it for him or herself the bulb is most conveniently placed at the side and not behind.

Two combinations may require to be used, a spirituous and an oily. The spirituous is that of wider applicability. The mixture which I have most largely made use of is one modified from a prescription by Dr. Charles J. White [*Journ. Amer. Med. Assoc.*, 1910, No. 13].

It consists of euresol 2 drms., spiritus formicarum 1 oz., spiritus rosmarini ½ oz., olei ricini ½ oz., spiritus vini rectificati to 8 oz.

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* This paper was received shortly before Dr. Jamieson's death, and is probably his last contribution to Dermatology.

Euresol is not at present available, as it is prepared apparently exclusively in Germany. It is an acetate of resorcin, and is met with as a syrupy liquid. For it, therefore, resorcin must be substituted, in the proportion of 1 drm. as against 2 of euresol. The main claim made for euresol as against resorcin is that it does not stain white hair, but this claim cannot be fully substantiated.

Should the scalp be reddened and its mobility interfered with, it may be necessary as a preliminary measure to reduce the inflammation and restore pliability by washing with superfatted fluid soap and using sulphur and salicylic pomades. When this has been accomplished, the period for the spray is reached. In case of dandruff or scurf, the spray may be commenced with at once. The mode of procedure is as follows: The scalp must be shampooed once a week or ten days, using for the purpose a mixture of fluid extract of quillaya in warm water, proportion varying from one teaspoonful to one dessertspoonful in half a washhand-basinful of warm water. This is poured on by means of a moderately large sponge and gently rubbed in. The scalp is then dried by means of a warm soft bath-towel. The spray is then used once or twice daily, twice at first, subsequently once. In this way the dandruff rapidly disappears. If the hair has been tending to fall out, the loss speedily diminishes, and is soon arrested more or less completely.

Should the scalp have become atrophied, no new hairs can be expected to reappear. But if it still retains its normal softness, new hairs will reappear.

While this constitutes the wider applicability of the spray, it may also be used as a lubricant in cases where the hair is too dry. When so employed the best medium available is oil of sesame, which has a high reputation among the natives of India as a hair-dressing. Combined with 10 gr. of resorcin to the ounce this oil may be sprayed on the scalp once every day, or less often as found necessary. The same treatment may be employed in the case of the beard when this region, as sometimes occurs, becomes affected by dandruff. On no account must the face be washed with soap, plain tepid water being used freely.

Other uses of the spray may be discovered, but the above are those which have proved most efficacious in my hands.

A CASE OF SYRINGOMA.

By S. NORMAN PAUL,
Sydney, N.S.W.

With Remarks by H. G. ADAMSON.

The patient, J. S—, is a man, aged 46 years. Situated over the left side of the sternum, 2 in. inside the left nipple and reaching to the mid-sternal line, there are about twenty-five smooth, firm, raised growths, the largest 2·5 cm. across and raised 1·5 cm. The growths are sessile, intimately associated with the skin, and move with it. The bases of the smaller nodules coalesce to form an infiltrated plaque (Fig. 1). The two largest growths have been present for twenty-five years, three others for twelve years, and a number have appeared in the past three years. In colour some show a decided dark blue, the remainder being either pink or pinkish-blue. Dilated vessels are coursing over the two larger growths, which appear cystic. The blue colour has been noticed only in the past twelve months. There are no enlarged glands. The patient has dyspepsia and states that, after an attack of dyspepsia, for several months past, a new growth has appeared and become painful, but otherwise there is no pain. The whole mass was excised and the blue coloration was found to be caused by blood, which filled the larger and some of the smaller cysts. The section shows the growth to be situated in the corium, lobulated, surrounded by fibrous tissue, and appears to be derived from the sweat-glands.

Diagnosis: (?) Adenoma of the sweat-glands.

REMARKS.

Dr. Paul's case at once excites interest on account of its unusual character (Fig. 1). It would be impossible to predict its histological structure from its naked-eye appearances, but microscopical sections were prepared by Dr. Paul, and from them (Figs. 2 and 3) he made the diagnosis of Syringoma.

The group of new growths to which Syringoma belongs comprises a number of types. It includes growths made up of embryonic basal cells in various stages of differentiation towards gland tissue.

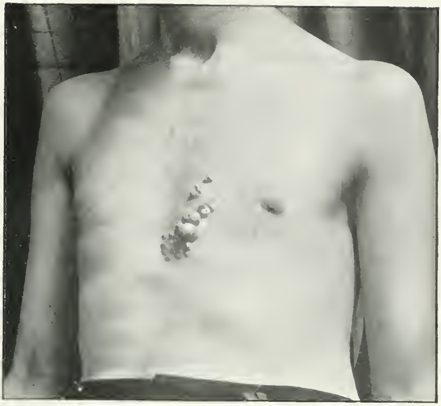

Fig. 1.—Photograph of a case of Syringoma (?).

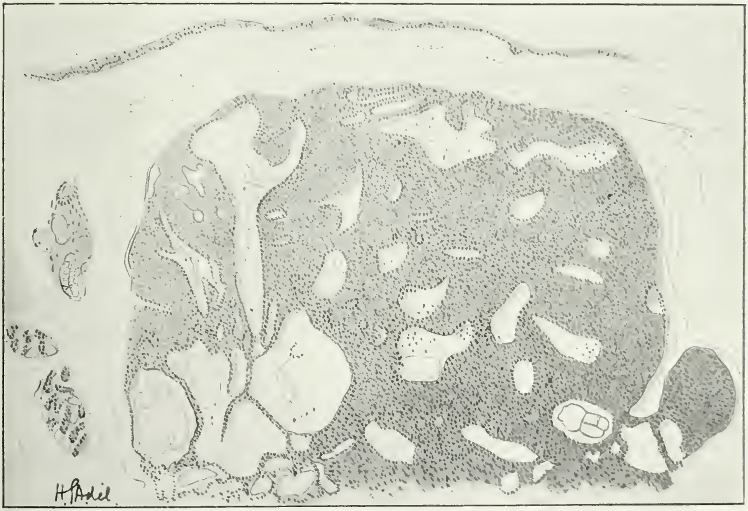

Fig. 2.—Syringoma (?). Drawing of a section of a small nodule. Under the low-power magnification the section recalls that of an adenoid epithelioma of the type of Brooke's "benign cystic epithelioma" (tricho-epithelioma, so-called), except that it is not divided into lobules.

TO ILLUSTRATE DR. S. NORMAN PAUL AND DR. H. G. ADAMSON'S ARTICLE ON A CASE OF SYRINGOMA.

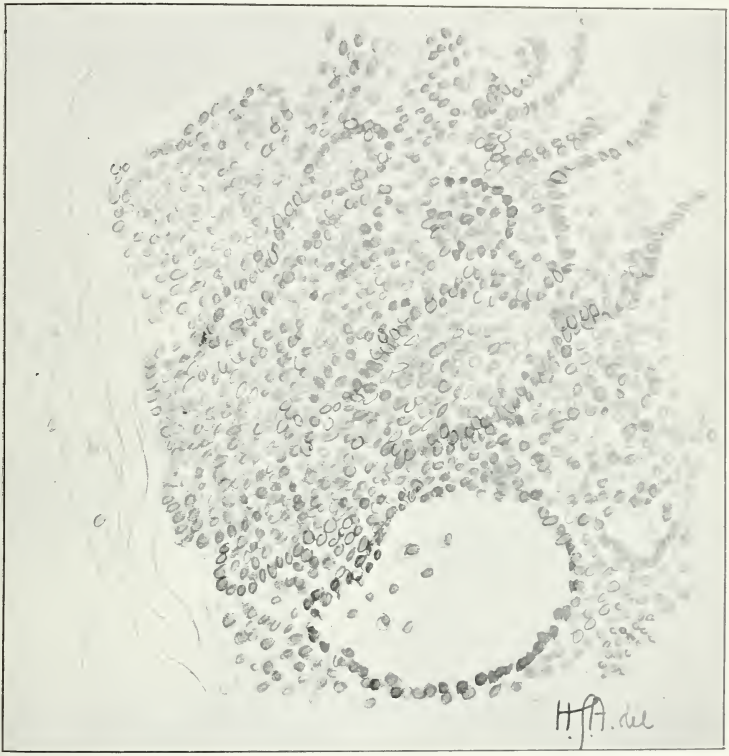

FIG. 3.—Syringoma (?). Drawing of the same section under a high power, which shows the tubule-like arrangement of the cell-growth and suggests the appearance of an adenoma of the sweat-glands, *i.e.* syringadenoma or syringoma, rather than that of an adenoma derived from pilosebaceous structures, *i.e.* epithelioma of Brooke or tricho-epithelioma.

TO ILLUSTRATE DR. S. NORMAN PAUL AND DR. H. G ADAMSON'S
ARTICLE ON A CASE OF SYRINGOMA.

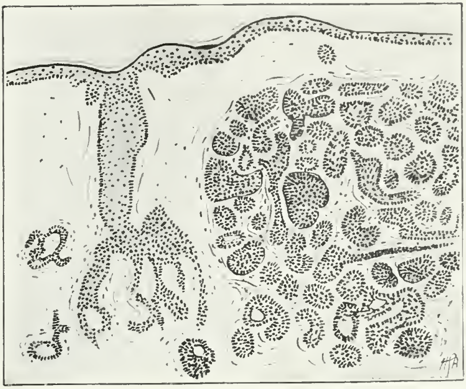

FIG. 4.—Section from a nodule on the forehead in a typical case of Epithelioma adenoides cysticum of Brooke. Contrasted with Figs. 2 and 3 it shows a lobulated tricho-epitheliomatous structure rather than a tubuliferous syringomatous character.

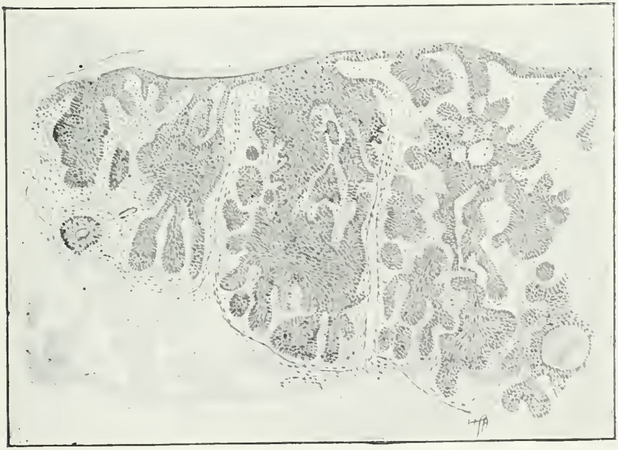

FIG. 5.—Section from a benign lower eyelid tumour for comparison with Figs. 2 and 3. It shows again a basal-cell growth of the tricho-epithelioma or embryonic pilosebaceous type. The resemblance to rodent ulcer is striking.

TO ILLUSTRATE DR. S. NORMAN PAUL AND DR. H. G. ADAMSON'S ARTICLE ON A CASE OF SYRINGOMA.

The growths may have the structures of fully developed gland tissue, in which case we call the tumour an adenoma: as Adenoma sebaceum and sudoriparous adenoma or sweat-gland tumours. They may be growths composed of more embryonic, less differentiated cells, as in Brooke's Epithelioma adenoides cysticum and in Lymphangioma tuberosum multiplex of Kaposi (*i. e.* Syringoma). They may be growths made up of basal cells which have lost all power of differentiation into gland-tissue cells and which have retained only that of proliferation, as in certain basal-cell epitheliomata, which we call rodent ulcer.

It seems probable that all these growths are derived from embryonic "cell-rests" as conceived by Cohnheim. Whether the cell-rest develops into an adenoma, into an adenoid epithelioma or into rodent ulcer, may perhaps depend upon the stage of development of the elements when the cell-rests were isolated, or perhaps upon the age of the patient at the moment the cell-rests become aroused into activity. It is conceivable that a glandular " cell-rest " which begins to grow during early life is more likely to develop into gland tissue than one which begins to proliferate only late in life. This question of the possible relationship between benign glandular tumours and rodent ulcer is one of considerable interest.

Since the case with which we are now concerned shows growths with no tendency to invade and destroy normal tissues or to ulcerate, we must place it among the benign forms, and, in order to know in which class to place it, it will be well to recall the already recognised types of adenomata and of adenoid epitheliomata.

The acknowledged types of these growths of glandular origin are:

(1) *Adenoma sebaceum*: in which there occur on the cheeks and sides of the nose and on the forehead little rounded tumours made up of sebaceous-gland tissue.

(2) *Epithelioma adenoides cysticum* of Brooke: in which the tumours are multiple and situate mainly on the face and especially about the forehead, temples, eyes and nose, but also on the scalp, neck and chest; and which is sometimes a family disease.

The structure of these growths is that of embryonic pilosebaceous follicles, so that they have been described as tricho-epitheliomata. Histologically the growths closely resemble rodent ulcer (Fig. 4) and it seems probable that rodent ulcer is also a tricho-epithelioma or embryonic pilosebaceous tumour, but made up of cells less stable than those of Epithelioma adenoides of Brooke and with, therefore, a greater tendency to break down and ulcerate.

(3 The multiple benign tumours of the scalp, the so-called *Endotheliomata of the scalp* of Spiegler, and Mulert, have been shown by Dubreuilh and Auché to be benign epitheliomata derived from the basal-cell layer of the epidermis and histologically to resemble rodent ulcer. In one of my cases of Epithelioma adenoides cysticum of Brooke, and in a case published by Freibos, these multiple scalp-tumours were associated with the face and body tumours. Freibos considers them to be syringomata, but I should agree with Dubreuilh in regarding them as pilosebaceous or tricho-epitheliomata.

(4) *Benign tumours of the lower orbital region* and of the naso-facial groove which have in many cases the structure of basal-cell epithelioma of the embryonic pilosebaceous or tricho-epithelioma type as in the illustration here given (Fig. 5). Jarisch's so-called "Hæmangioendothelioma" was probably of this nature. Other of these growths are probably of embryonic sweat-gland origin, as in Darier's "Hidroadénomes des paupières inférieures."

It is becoming now a widely accepted view that rodent ulcer (which occurs so frequently in this situation) is a growth of embryonic pilosebaceous gland origin, or in other words a malignant tricho-epithelioma. It is an interesting question whether rodent ulcer may be sometimes of embryonic sweat-gland origin, *i.e.* a malignant syringoma; but there is certainly less resemblance between the histological structure of a rodent ulcer and that of a syringoma than there is between that of rodent ulcer and benign tricho-epithelioma.

(5) An important type, probably of embryonic sweat gland origin, is that originally described by Kaposi as "Lymphangioma tuberosum multiplex," and later by Jacquet and Darier as "Hydradénome eruptif," by Török as "Syringo-cystadenoma," by Gassmann as "Nævi cyst-epitheliomatosi disseminata" and now generally known by the name given to it by Unna, of Syringoma or Syringadenoma.

Cases of this type have been frequently confused with Brooke's "Epithelioma adenoides cysticum," which, as we have seen, is now regarded as an embryonic pilosebaceous gland tumour. But they differ from Brooke's type in that the tumours are situated on the chest below the clavicle rather than on the face and scalp, in that they do not occur as a family affection, and in that their histological structure has a more tubular arrangement which recalls the tubules of an embryonic sweat-gland.

(6) Single tumours in various situations have been described as *sweat-gland tumours, sudoriparous adenoma,* or *Syringoma.* Unna quotes several cases by older writers as being genuine examples of sweat-gland adenoma. Darier and Fordyce have collected and reported cases (Darier, a case of multiple tumours), and Wolfheim, Torok, Blaschko, Rolleston, and others have described benign or malignant tumours of sweat-gland origin.

It is not always clear whether these writers are dealing with tumours which show a frankly tubular arrangement so that they could be recognised as sweat adenoma, just as we recognise sebaceous adenoma, or whether they are tumours which merely suggest a sweat-gland origin as in the type of multiple tumour which Kaposi described as Lymphangioma tuberosum multiplex, and which we now generally call syringoma.

It is interesting to note that some of these observers have recorded cases of sweat-gland tumours becoming malignant, but whether the malignancy is of the type of rodent ulcer is not quite apparent.

(7) Lastly, there are a few recorded examples of linear nævus made up of sweat-glands or of sebaceous glands.

Dr. Paul's case may, I think, be excluded from the group of pilo-sebaceous or tricho-epitheliomata. Although it has not a pronounced gland structure it may, perhaps, be placed among the sweat-gland tumours of class 6. The massing of the growths in one area is suggestive of a segmental or linear nævus, and unlike that of the typical case of "Lymphangioma tuberosum multiplex" of Kaposi. It is closely similar in appearance and in its histological structure to a case of "Hypertrophic u. multiple Cystadenoma der Schweissdrüsen" recorded by Thimm.*

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* *Arch. f. Derm. u. Syph.*, 1904, lxix, Hft. 1 and 2, p. 1. (The photograph and coloured drawing of Thimm's case reproduce almost exactly the appearances of Dr. Paul's case, and the microscopical sections seem to show very similar features.)

DIPHTHERITIC WHITLOW.*

By J. D. ROLLESTON, M.D.

A boy, aged 5 years, was admitted to hospital on October 6th, 1915, with severe faucial diphtheria on the third day of disease. Twenty thousand units of antitoxin were given on admission, 16,000 on October 7th, and 12,000 on October 8th. The throat became clean on October 11th. An urticarial rash appeared at the injection site on October 12th and persisted till October 15th.

The same day the heart, hitherto normal, showed some left-sided dilatation and an occasional extra-systole, and the child vomited. On October 16th triple rhythm developed, and the liver became enlarged. On November 2nd the voice became nasal. The following day a circinate rash appeared on the limbs.

On November 4th, the thirty-second day of disease, he developed a transient right hemiplegia and aphasia, and on the same day the left index, middle, and ring fingers each showed a bulla on the terminal phalanx, the appearance presented being very similar to that caused by a burn. The voice remained nasal until November 29th, but no other nervous symptoms developed, and when he was allowed up on December 3rd, the sixty-first day of disease, he was able to walk without support. In spite of a variety of local applications, such as 2 per cent. solution of iodine, fomentations, compresses of sodium citrate and sodium chloride, and iodoform, the lesions in the fingers showed little tendency to heal. Profuse discharge occurred from the granulations that had formed after the bullæ had been snipped. Sloughing took place, especially in the middle finger, and a greater part of the nail of the middle finger and some portion of the nail of the index became loosened and were removed. Subsequently a rudimentary nail formed on the middle finger just above the ordinary situation.

Except when the fingers were dressed the child did not complain of any pain, and there was no rise of temperature nor any constitutional disturbance.

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* The case was shown at the Section for the Study of Disease in Children of the Royal Society of Medicine on March 24th, 1916.

No membrane was seen at any time, and the lesions were indistinguishable from an ordinary severe whitlow.

It was not until January 19th that the possibility of the lesions being diphtheritic occurred to me, and a culture was taken from the discharge of the middle finger. Numerous groups of diphtheria bacilli were found; 8000 units of antitoxin were injected and within a week the lesions, which had been in existence for two and a half months, had completely healed.

The child contracted a severe attack of chicken-pox on January 26th, which necessitated his detention until March 13th.

On his discharge from hospital on that day the left index, ring, and especially the middle finger, showed some deformity and ulnar deflection of the terminal phalanges. There was marked limitation of movement of the terminal phalanges of the index and middle fingers, from which nearly all the nail had disappeared.

The nail of the ring finger showed a deficiency on the ulnar side only.

Diphtheria of the skin, secondary to diphtheria of the fauces, nose, and larynx, or other mucous membranes, though more frequent than primary cutaneous diphtheria, is by no means common nowadays.

In a series of 2600 cases of diphtheria which were under my care at the Grove Hospital between 1902 and 1914, only 30, or 1·1 per per cent., showed any cutaneous involvement, the distribution of which was as follows: Philtrum, 12 cases; pinna, 5; fingers, 2; external malleolus, 2; umbilicus, groin, prepuce, anus, perineum, labium majus, axilla, cheek, lower lid, 1 each.

The great majority of these were severe cases, two of which, as examples of multiple and unusual localisations of diphtheria, I have recorded at length elsewhere (12).

Similar figures are given by Adler (1), who states that only 23 cases of diphtheria of the skin, or 1·04 per cent., occurred among 2217 diphtheria patients treated at St. Anne's Hospital, Vienna, from 1894 to 1902.

In all my previous cases the cutaneous lesions were coexistent with the angina, and presented typical diphtheritic membrane.

The present case is the first I have seen in which cutaneous diphtheria first developed after the throat had become clean. There was, in fact, an interval of more than three weeks between the disappearance of the faucial membrane and the onset of the skin affection.

This is all the more remarkable as the child, in accordance with the practice prevalent in most of the Metropolitan Asylums Board hospitals, had been treated with enormous doses of antitoxin, and is an illustration of the fact that ordinary anti-diphtheric serum possesses little or no bactericidal power.

The question arises as to whether the whitlows were diphtheritic from the first, or whether the presence of the diphtheria bacilli was due to a secondary infection. As no culture was made until the lesions had been in existence for two and a half months a definite answer cannot be given.

I was at first inclined to regard the presence of the diphtheria bacilli as a superadded infection, especially as at no time was there any trace of diphtheritic membrane.

A study of the literature, however, has induced me to support the opposite view. Several cases have been reported, *e.g.* by Cross (2), Seitz (13), Hau (8, 9), Garratt (6), Eddowes (4), and Dawson (3), in which cutaneous diphtheria was bullous from the first.

Hau (8), of Lyons, who was the first to describe diphtheritic whitlow under the term "panaris diphtérique," drew attention to the absence of typical diphtheritic membrane in many of his cases, and states that the lesions resembled those produced by a blister, and Knowles and Frescoln (10), in a recent article on cutaneous diphtheria, speak of a special bullous type of diphtheria of the skin.

The polymorphous character of cutaneous diphtheria has also been illustrated by de Verbizier (16) in an article on pyodermia due to diphtheria bacilli.

There is no doubt in my mind that, whether the diphtheritic infection of the whitlows was primary or secondary, the Klebs-Loeffler bacillus played an important part in the persistence of the lesions, as shown by their rapid healing after injection of antitoxin.

The obstinate and misleading nature of the lesions, and the readiness with which they yielded to specific treatment, find a parallel in cases of digital chancres, which are not infrequently mistaken for ordinary whitlows.

A similar instructive case, which also shows how those familiar with diphtheria may be slow in recognising a diphtheritic lesion of the finger, has been recently recorded by Dr. F. E. Tylecote (15). When resident in a fever hospital one of his colleagues had a troublesome onychia which refused to heal in spite of antiseptic and cauterising treatment extending over some weeks. Like my patient he had no temperature, but "looked toxic and complained of feeling run down."

Cultures of the discharge gave a pure growth of Klebs-Loeffler bacilli; 4000 units of antitoxin were given, and in about five days the local condition had healed, while he rapidly gained his strength, without any subsequent paralysis.

It is probable that many of the cases of obstinate whitlow occurring in hospital residents and nurses are diphtheritic in origin.

Doctors may become infected during performance of an autopsy or intubation, as in cases reported by Hau (8, 9) and Emge (5), while nurses are liable to be bitten while cleaning the mouths of their patients.

The nurse in charge of the present case reminded me that I had treated her some years previously for a troublesome whitlow which she had contracted while on duty in a diphtheria ward. In spite of various local applications it had persisted for several months, but the absence of any membrane had prevented my taking a culture.

The loss of tissue was less than in the boy's case, and no deformity or any sequelæ, nervous or otherwise, resulted, but on retrospective consideration it seems probable that her whitlow was also due to the diphtheria bacillus.

The chronicity of unrecognised cutaneous diphtheria has been noted by several observers, the most remarkable example being that published by Slater (14), in which the lesions, resembling a generalised herpes, persisted for three years, but rapidly healed after injection of antitoxin.

The neurological aspects of my case will be discussed at length elsewhere, but it is worth noting that no nervous sequelæ resulted such as were recorded in the pre-antitoxin era by Paterson (11) and Guthrie (7) following diphtheritic lesions of the fingers without faucial involvement.

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A NEW TEST FOR SYPHILIS (THE EMULSOID-GELATION, OR THE "GEL" TEST).*

BY J. E. R. McDONAGH, F.R.C.S.

THE "gel" tests, as I have called them for short, since the change observed is the conversion of the emulsoid particles, which form the internal phase of the serum, into gel particles, give more accurate results than can be obtained with the Wassermann reaction. In the first place, it is easy to distinguish one syphilitic serum from another, *i. e.* a serum withdrawn in the early stages of the disease gives a different reading to one in the late stages. Secondly, the influence of treatment upon the solid particles or the protective substances in the serum can be better gauged. Thirdly, paradoxical results are not obtained, results which are too often met with in the non-specific complement-fixation test, especially with sera from patients who have recently been treated. Fourthly, a positive reaction is never obtained with a normal serum, provided it has not been kept too long, and negative reactions are not given by the "gel" tests, when the results should have been positive.

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* At first I thought the colloidal transformation was emulsoid-suspensoid, but since I have discovered that the precipitate is soluble in water, the change must be one of gelation.

Every serum subjected to these new tests—and there have been 200 in all—has also had a Wassermann reaction done. Out of these 200 cases, one gave a strong positive and two a slight positive Wassermann reaction, although the patients had never had syphilis, so far as one was able to tell. By the "gel" tests these sera were normal. Thirty-seven of the 200 cases gave a negative Wassermann reaction, when the test should have been positive. By the "gel" tests all these sera were positive.

I propose in this short article only to describe the methods of doing the tests and the results obtained, when compared with the Wassermann reaction. Those desirous of learning the evolution and *rationale* of the emulsoid-gelation reaction will find them fully described in my recent book.* It is not necessary to employ all the methods described when testing a given serum, and each observer will discover in time which one he finds the most suitable. If more than one is used, it naturally serves as a check to the other.

TECHNIQUE COMMON TO ALL THE TESTS.

Blood is taken from the vein and the serum allowed to separate off. The serum should for preference be clear and free from blood, but an opaque serum or one tinged with hæmoglobin will still give satisfactory results. The serum will give the reaction so long as it has not undergone decomposition, consequently it may be kept for a few days.

When performing the test it is necessary to have a known negative serum as well as a known positive serum, because the time of year and the temperature of the room make a slight difference to the readings. For each serum three dry test-tubes are taken and marked 1, 2, 3. Into the first tube 2 drops of serum are placed, into the second tube 3 drops, and into the third tube 4 drops. The drop pipette is best made from narrow-bore glass tubing, to ensure that each drop is as small as possible. As the results obtained depend upon the size of the drop used, it is, of course, imperative that the same pipette should be used for each series of tests. The pipettes can be standardised by weighing the drops on a torsion balance. If the drop is the same for each series of tests, it does not matter whether in one series the drop is larger or smaller than that used in another series, provided every series contains a positive and negative control; but, of course, the readings will vary accordingly. The results can be read off at once and again the next day. In the interim the tubes must be left at room temperature, and not incubated. Incubation sends some of the precipitated protein into solution, hence it makes the variations less distinct, and the results are then difficult to read.

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* *Links in a Chain of Research on Syphilis*, Harrison & Sons, London.

Acetic Acid Ammonium Sulphate Test.

Requirements: (1) Pipette divided into c.c.'s.
(2) Pipette divided into tenths of a c.c.
(3) Glacial acetic acid.
(4) Acetic anhydride.
(5) Saturated solution of ammonium sulphate.

To keep the ammonium sulphate solution saturated it is a good plan to have the bottom of the bottle covered with crystals.

To each of the three tubes containing their respective quantities of serum 0·1 c.c. of acetic anhydride and then 1·0 c.c. of glacial acetic acid are added. When the tubes have been well shaken, a drop of ammonium sulphate is added to each. The tubes are again well shaken, when a mass of crystals appear (probably ammonium sulphate). The density of the opacity is then noted, and the reading taken again next day, when a precipitate has formed and the crystals have become deposited.

The following tables give the reading of a normal serum taken at once and twenty-four hours later.

Normal Serum.

Tube	1	2	3
First reading . . .	+* .	− − + .	− − +
Second reading, 24 hours later	f.p. .	(f.p.) .	+ +

* + + + + means a dense opacity. — means that the solution is clear like water. f.p. means a dense flocculent precipitate. (f.p.) means a flocculent precipitate which is not complete.

Syphilitic Serum.

Tube	1	2	3
First reading	+ + +	+	+
Second reading, 24 hours later	f.p.	f.p.	f.p.

According to the size of the drop used a variation may be found in the amount of crystals which form in a syphilitic and in a normal tube. In all the tubes at first crystals form, but in the normal tubes they often disappear in 6–24 hours, while they remain in the syphilitic tubes.

ACETIC ACID LANTHANUM SULPHATE TEST.

Requirements.—Same as the preceding test with two exceptions. In the first place acetic anhydride is not required, and a saturated solution of lanthanum sulphate in glacial acetic acid is used in the place of ammonium sulphate.

After the serum has been added to the tubes containing 1·0 c.c. of glacial acetic acid, 0·2 c.c. of the lanthanum solution is placed in each.

Normal Serum.

Tube	1	2	3
First reading	+	—	—
Second reading, 24 hours later	+(+)	—	—

Syphilitic Serum.

Tube	1	2	3
First reading	+++	+	—
Second reading, 24 hours later	f.p.	+ +	+

This test can be made more delicate and the results can be read quicker if the following procedure is adopted:

To 2·0 c.c of glacial acetic acid, 0·5 c.c. of serum is added. Four test tubes are then taken containing 1·0 c.c. of glacial acetic acid in each. Into the four tubes, two, four, six, and eight drops of the acid serum are placed respectively.

Normal Serum.

Tube	1	2	3	4
First reading in about 10 minutes	+	+ +	+ + +	+ + + +
Result in 1 hour	+	+ +	(f.p.)	(f.p.)

Syphilitic Serum.

Tube	1	2	3	4
First reading in about 10 minutes	(f.p.)	(f.p.)	(f.p.)	(f.p.)
Result in 1 hour	(f.p.)	(f.p.)	f.p.	f.p.

ACETIC ACID THORIUM SULPHATE TEST.

Requirements.—Same as in the preceding test, only the lanthanum sulphate solution is replaced by a saturated solution of thorium sulphate in glacial acetic acid.

To each tube containing 1 c.c. of glacial acetic acid its respective amount of serum is added, the tubes are well shaken, and then 0·2 c.c. of the supernatant fluid in the thorium sulphate solution is added.

Normal Serum.

Tube	1	2	3
First reading	f.p.	− +	−
Second reading, 24 hours later	f.p.	+	− +

Syphilitic Serum.

Tube	1	2	3
First reading	f.p.	+ +	+
Second reading, 24 hours later	f.p.	(f.p.)	+ +

ACETIC ACID THORIUM NITRATE TEST.

Requirements.—Same as in the preceding test, only the thorium sulphate solution is replaced by a saturated solution of thorium nitrate in glacial acetic acid. The test is carried out in the same way and 0·2 c.c. of the clear thorium nitrate solution is added to each tube.

Normal Serum.

Tube	1	2	3
First reading	f.p.	(+)	–
Second reading, 24 hours later	f.p.	+ +	+

Syphilitic Serum.

Tube	1	2	3
First reading	f.p.	+ + +	+
Second reading, 24 hours later	f.p.	f.p.	+ + +

During the last few years more reliance has been placed upon the Wassermann reaction than upon clinical experience, and I am of the opinion that the time is not far distant when the Wassermann reaction will be found to be far less specific than is now thought to be the case. I am convinced in my own mind that a positive Wassermann reaction in the majority of cases only signifies that the patient has had syphilis, not that he is actively syphilitic or that he even requires treatment. Whether the "gel" tests will do more than confirm the clinical diagnosis, only the future will show.

A CASE OF FOURNIER'S SECONDARY SYPHILITIC ANALGESIA.

(*Clinical Notes from the Skin-Department, Rigshospital, Copenhagen. Director, C. Rasch.*)

By C. RASCH.

(Translated from the Danish by W. JENKINS OLIVER.)

Anyone who has heard Fournier's lectures or who has read his "Traité de la Syphilis" will know that under the name of *Analgésie secondaire* he has described a phenomenon which is occasionally observed in the early stages of syphilis, most frequently in women. It appears either as distinct analgesic areas which have a fixed situation, occurring symmetrically on the dorsal surfaces of both hands and on the mammæ, more rarely as irregular and unilaterally distributed patches, or as a combination of analgesia and anæsthesia. There is seldom found an accompanying thermo-anæsthesia. They appear either in conjunction with other syphilitic manifestations or as the only lesion, and persist for several months. They differ from hysterical and functional analgesias in their symmetrical distribution, their preference for the regions mentioned, only rarely being found together with hyperæsthetic phenomena, and in their only seldom being observed on the mucous membranes. Since this symptom does not appear to be very well known by, nor to have received much attention from syphilologists and neurologists, the following case may be of some scientific and practical interest.

A young girl, aged 21 years, was admitted with syphilis into the Skin-Department of the Rigshospital on August 30th, 1915. She was unable to say exactly when she had become infected, but had first noticed in October, 1914, some ulcerations on the forehead, for which she was treated in the Department for Skin and Venereal Diseases of the Kommunehospital, with thirty-nine inunctions of mercury. In March, 1915, an ulcer appeared in the throat, which was treated at the same institution with other thirty inunctions up to the end of April, since which date she had received no further treatment. In the middle of July some ulcerated sores again began to appear on the forehead; at the same time she suffered from headaches, considerable shedding of the hair, much loss of weight, and inability to take her food.

On admission the patient was very thin and pale. On the frontal border of the hairy scalp was a sharply-defined flat ulcer, in size rather larger than a florin. On the face and beneath the chin were four other smaller ulcers of the same appearance, with a fifth to the right of the vertebral column immediately above the vertebral border of the spina scapulæ. All the lesions were freely movable on the underlying parts; no bone affection could be observed. There were no other syphilitic manifestations on the skin except a considerable loss of hair. No recognisable enlargement of the lymph glands; nothing abnormal about the genitalia. On the left tonsil, however, was a sharply-defined ulceration of the size of a hazel-nut, with a yellow covering. Wassermann's reaction was positive. Auscultation revealed nothing abnormal, no tubercle bacilli in the sputum; weight was 45 kgrm. Owing to the very poor general condition of the patient a tonic containing iodide of potassium and iron was prescribed, under which treatment the sores healed in the course of three weeks and she gained some 5 kgrm. in weight. From September 23rd she had been taking, in addition, infusion of sarsaparilla. Examination of the spinal fluid on September 9th showed normal conditions (Wassermann's reaction negative, 1 cell per c.mm.; protein (Bisgaard), 0–10). In the blood, Wassermann's reaction, on September 9th, was positive; on September 23rd, negative; and on September 30th, positive. Nothing abnormal was shown by an ophthalmological and otological examination. Hæmoglobin, 75–80 per cent.

As the patient, in spite of the fact that her general condition improved, continued to look pale and nervous, on September 30th I tested her sensations on "Fournier's areas," and found a pronounced analgesia on the dorsal surfaces of both hands and on the mammæ, accompanied by some anæsthesia. At my request she was then thoroughly examined by our neurological department, when the following report was furnished: Pupils equal, and react to light. Cranial nerves on the whole show nothing abnormal. Upper extremities—no atrophy, muscular power about the average, tendon reflexes brisk. There is hyperæsthesia and hypalgesia of the glove type, with the upper limit about the middle of the forearms. No alteration in the sense of localisation or of passive position. Trunk—over the lower part of the vertebral column is a bow-shaped kyphosis which it is difficult to straighten; no paresis of the abdominal muscles; hypæsthesia and hypalgesia over both mammæ. Lower extremities—no atrophy nor paresis. There is hypæsthesia and hypalgesia on the thighs and upper part of the legs on their anterior aspects. The patellar reflexes are entirely absent, even with reinforcement. On the other hand, the Achilles tendon reflexes on both sides are brisk, the plantar reflexes normal (according to my own observation there was definite downward movement). No affection of the senses of localisation, nor of passive position. According to the patient's own statement the hypæsthesia on the legs is greater than that on the hands. Conclusion—the absence of the patellar reflexes definitely points to an affection of the nervous system, and together with the altered sensation on the lower limbs suggests chiefly an affection of the cord rather of the nature of some slight vascular disturbance than a meningitis. The altered sensation on the upper limbs, on the other hand, can only be explained by being functional in origin, while the hypæsthesia on the mammæ might be due to either cause.

As a result of this examination a lumbar puncture was again performed, and this showed the same condition of the spinal fluid as before, with the exception that now there was present an increase of the protein content (1–40, Bisgaard).

Fournier's analgesia has in this case therefore been of value in putting one upon the track of a previously overlooked affection of the central nervous system. It is also worthy of note that this condition occurred without a trace of any leucocytosis in the spinal fluid, which on the first examination was completely normal. Although the spinal fluid is known in the majority of cases of syphilitic conditions of the central nervous system to show more or less pronounced changes (especially leucocytosis), cases are known to occur without these alterations. It is also evident that affections inside the brain and cord (which is shut off from the spinal canal) may exist without producing any changes in the spinal fluid.

Of these figures, referring to the protein content of the spinal fluid, the first indicates the globulin fraction, the second the total albumin content. Normally the numbers are 1–2 and 10–20 respectively.

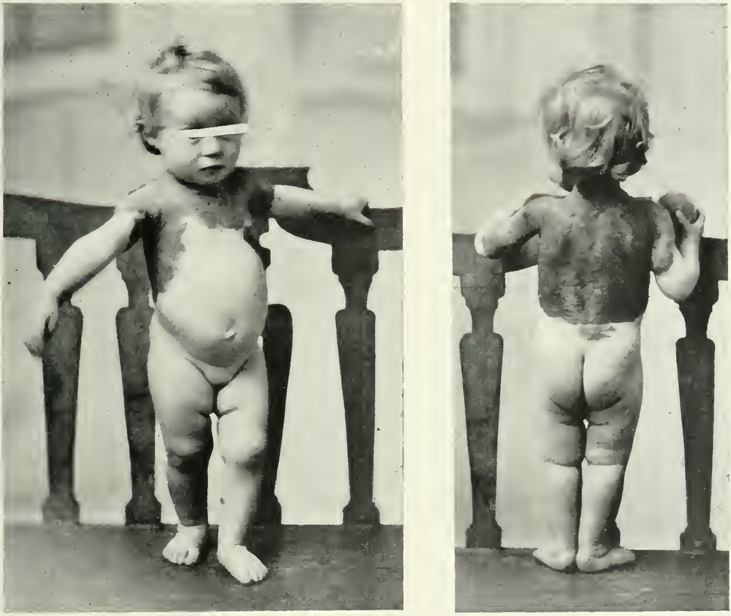
CLINICAL NOTE.

AN UNUSUAL CASE OF EXTENSIVE PIGMENTED HAIRY NÆVUS.

By GEORGE PERNET, M.D.,
Dermatologist to the West London Hospital and Lecturer on Dermatology, West London Post Graduate College.

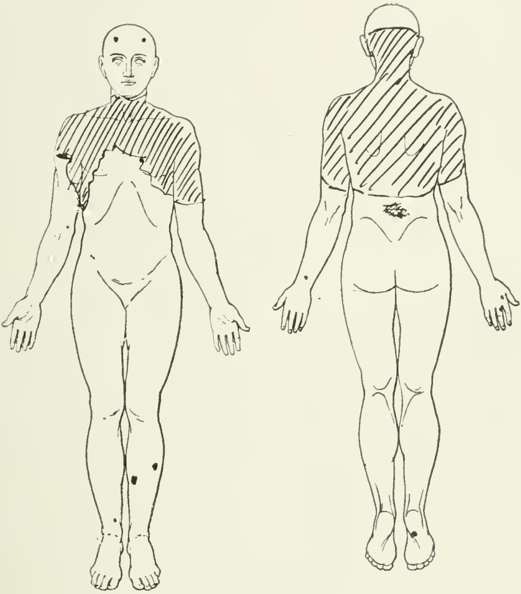
The subject of this short note is a girl, aged 1 year and 7 months, who was first seen in December, 1914. The child was brought to the Hospital for a mild pus infection of the skin, and was then seven months old.

The extent of the pigmented hairy nævus is shown in the two photographs, but as far as the back view is concerned, the upper part of the nævus is concealed by the hair of the head. In that situation it reached up to an almost straight transverse line on a level with the



TO ILLUSTRATE DR. GEORGE PERNET'S CASE OF EXTENSIVE PIGMENTED HAIRY NÆVUS.

tips of the ears, like a turned-up fur jacket coat-collar. The nævus was darkly pigmented. The hair on it was quite two inches long in parts, especially about the back, fine and silky, and pale in colour. Scattered about the body there were a few pigmented nævi, two of them being symmetrically situated in the scalp in front near the hairy margin and within it (*vide* diagrams). One of the two small nævi on the outer side of the left leg had been selected for vaccination.



Extensive pigmented hairy nævus to show distribution.

The usual maternal impression was forthcoming, but that need not detain us. *Vita brevis.* More important was the fact that an examination of the mother revealed radiating linear scars about the lips and angles of the mouth, pointing to congenital lues. The present child was the only one. No miscarriages. The question was put as, in congenital lues, miscarriages are not at all uncommon, it may be said in passing.* As some readers will be sure to ask as to the Wassermann, the mother's blood was incompletely positive and the baby's slightly suspicious (Dr. Elworthy, Pathologist to the West London Hospital). Clinically I had no doubt about the congenital lues of the mother.

Last November (1915) the left leg was noticed to be distinctly smaller in diameter than the right, and the mother stated the child dragged it when she tried to walk. The photographs taken in December, 1914, do not show any difference in the two legs, nor was dragging complained of then. The diagnosis was anterior poliomyelitis, and this was confirmed by Dr. Arthur Saunders in the Children's Department of the Hospital.

ROYAL SOCIETY OF MEDICINE.

DERMATOLOGICAL SECTION.

MEETING held on February 17th, 1916, Dr. J. H. STOWERS, President of the Section, in the chair.

Dr. E. G. GRAHAM LITTLE showed a case of *sclerodermia associated with Graves's disease, and later myxœdema, benefiting conspicuously by implantation of human thyroid into the bone marrow.* The patient was an English lady, aged 52 years, the wife of an Irish Army officer. Her home in Ireland was very damp. In January, 1902, she was under the care of the late Sir William Broadbent and also of Sir Thomas Barlow, and presented symptoms of tachycardia, anæmia, and dilatation of the heart, but there was then no exophthalmos or apparent thyroid affection. About this date also there were severe pains in the fingers and shoulders, suggesting a neuritis. She was seen again in 1907 by Sir Thomas Barlow, who had a note in January, 1907, that the thyroid was normal, but the other symptoms pointed to a "half-developed exophthalmic goitre." The hands were stated by the husband, who kept a careful diary of his wife's condition, to have been "puffed, stiffened, and dead." About this time, too, Sir Thomas Barlow noted brawny swellings below the lower eyelids, variable, feeling hot, and somewhat resembling a chronic urticaria, "such as is found in people with a gouty diathesis. It was certainly not a typical myxœdema." There was a good deal of pigmentation as well. In January, 1908, she had a bad attack of "influenza." In March, 1908, she was seen by Prof. Ashley Cummins, of Cork, who made a definite diagnosis of myxœdema and administered thyroid by the mouth in the form of dried extract. A little later in the same year she was seen by Sir Thomas Barlow, whose note in October was to the effect that the thyroid was enlarged, especially on the right side, the heart was "murmurish," the pulse-rate 120, and there was much anæmia. Periods of irregular pyrexia with "urticarial" swellings, as noted before, and very severe pains in the shoulders and neck, rheumatic affection of tissues round finger-joints, elbows and shoulders (fibrositis ?) were also now recorded.

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* See Pernet, "The Offspring of Congenital Syphilitics," *Brit. Journ. Derm.*, vol. xi, 1899, p. 459. See also Discussion, Paris Congress Dermatology, 1900, *Transactions.*

These pains and affections of the joints rendered her incapable of walking, and she was carried in a chair. The symptoms were always worse in damp weather. There was no deformity or overgrowth of bone. In January and February, 1909, she was again under Sir Thomas Barlow for a very curious parotitis, first of one side and then of the other. There was apparently a slight block in the duct, and the gland became swollen and tender, especially under the stimulus of savoury cooking. There was always some fever with these attacks lasting a few days, not more than a week; there was never any suppuration, but there was pain and difficulty in moving the jaw. These attacks were frequently repeated during the subsequent eighteen months. The first definite diagnosis of sclerodermia, which was probably foreshadowed in the "neuritic pains in the fingers," was recorded in June, 1910, affecting chiefly the fingers, forearms, face, and thighs. These symptoms became so pronounced that she was unable to dress herself or write, and was practically crippled. She was treated at Droitwich, with perhaps some benefit, and later with sulphur baths at Biskra. Here she made the acquaintance of Prof. Kottmann, of Berne, who persuaded her to seek the advice of Prof. Kocher, which she did in May, 1911. Sir Thomas Barlow, in a letter dated May, 1911, wrote to Kocher a long summary of the facts detailed above, and commenting especially on the condition of the thyroid, said: "My opinion is that on the whole it has shown some degree of atrophy, but it is not easy to say how far the wasting is proportional to her general wasting [which was very marked]. She has had very considerable anæmia with a certain amount of pigmentation. This at times has been very marked indeed, almost bad enough for a pernicious anæmia. As to treatment, I think it cannot be denied that some benefit has resulted at times from thyroid extract, but it has never been considerable, and I am of opinion that at times it has exhausted her. Various forms of hot bath applications have been beneficial, and massage has at times helped her, but the permanent results of therapeutics have, it must be confessed, been limited indeed. I have never seen any case of pure myxœdema behave like this." And the mental accompaniments of myxœdema, the lethargy and dulness, were certainly conspicuously absent. The first implantation of thyroid was made by Kocher in Berne in May, 1911, the thyroid being removed from a case of goitre and immediately transferred to the bone marrow of the tibia through an incision in its anterior surface. She was seen immediately on her return in June, 1911, by Sir Thomas Barlow, who noted that the wound in the leg was unhealed, that she could walk about, that her colour was better, and the movements more free, but that she could not move the jaw owing to the immobility of the skin of the face. There was no parotitis. The sclerodermia was very much better. In November, 1911, Sir Thomas had the following note: "The isthmus of the thyroid can be felt. Sclerodermia much less; for example, she can pick up a pin, but there is still some tightening of the skin, the palmar fascia is thickened, the extremities are cold, left less than the right."

She was taking, on Kocher's orders, from the date of the operation, small doses of iodothyrine, which seem to have suited her better than thyroid extract. In February, 1912, she made a second visit to Kocher, who performed a second implantation of thyroid, also from a goitrous subject, into the marrow of the other tibia. After the operation she got a chill and developed a right lobar pneumonia and nephritis with scanty urine containing 25 per cent. albumin. On March 22nd, 1912, Dr. Albert Kocher, son of Prof. Kocher, wrote to Sir Thomas Barlow: "As to the condition of the sclerodermia, it is difficult to judge as yet whether it is any better. We think she ought to go on with the iodothyrine for the present. We gave her, three times [a day ?], 0·05 gr., but we think that she may soon go down to 0·05 gr. once [a day ?]." She appeared to have been taking this dose almost constantly ever since. Exactly a year later, in February, 1913, she was taken for a third visit to Kocher, who however did not operate, but administered "a new drug," according to the husband, which made her very ill with heart attacks, and this administration was stopped after ten days' trial, when iodothyrine was again resumed.

In June, 1913, the patient was "very ill," and was seen by Prof. Ashley Cummins, who apparently diagnosed a Pyorrhœa alveolaris, and ordered vaccine injections, of which she had twelve, with benefit. In September, 1913, she had an attack of Herpes zoster, and was seen later by Sir Thomas Barlow, who, in consultation with Mr. Oddy, advised the removal of all the teeth. This, according to the husband's narrative, was followed by a notable improvement in every way in her general health and appearance, an improvement which has been steadily maintained.

Menstruation ceased in 1908.

Present condition: The patient was anæmic and thin, but active and alert. The areas where sclerodermia was noted had improved to the degree of practical cure of the glossy skin and tightening effect, except on the hands and fingers, where the fingers were partially atrophied, and the skin over them was very shiny and tense, but without contracture, the fingers being sufficiently mobile to allow of her playing the piano. There were on the face very numerous telangiectatic patches about $\frac{1}{4}$ in. in diameter, which apparently varied in intensity, but never quite disappeared. She was also suffering from several corns on the plantar surface which impeded walking, which, however, was nevertheless freely undertaken. She expressed herself as incomparably better than before the thyroid implantations, when, as had been mentioned, she had to be carried everywhere in a chair. The skin of the face was supple and otherwise normal, and this was a great relief, as she said complaints had previously been frequent when she was staying at hotels that her corpse-like, rigid face disturbed the other guests.

Comments.—The coincidence of sclerodermia with thyroid disorders had long been observed, but great differences of opinion had been expressed as to whether the association had been more frequent with hyperthyroidism (Graves's disease) or with hypothyroidism (myxœdema.) In a recent communication to this Section, Dr. Sequeira described a case associated with myxœdema, and in the present case the symptoms of sclerodermia were certainly more pronounced in the stage of diminution of thyroid activity, and seemed to have progressed *pari passu* with that.

It was obvious that he owed a special meed of thanks for very generous help to Sir Thomas Barlow, his venerated colleague for the past ten years in the representation of medical graduates on the Senate of the University of London. He had allowed him to reproduce his notes, and had taken infinite trouble in looking up his records in innumerable case-books over this long period during which this lady had been under his observation. He felt sure the Section would wish to thank him for the resulting fulness and interest of this unique record.

The PRESIDENT said that this case was exceptionally interesting, partly because of the combination it presented and partly because of the long observation of the case by Sir Thomas Barlow. He would like to know what was the vaccine used, and whether any observations had been made on the patient's blood.

Dr. KNOWSLEY SIBLEY said he would be glad to know what dose of thyroid the patient was taking before the implantation of thyroid was carried out; also whether she tolerated it well by the mouth.

Dr. F. PARKES WEBER pointed out that one of the patient's earliest symptoms was the tendency of the hands, especially the fingers, frequently to become numb, white, and cold. That was the way in which the "sclerodactylia form" of sclerodermia most frequently commenced, he believed. It was later on that the contraction and cicatricial changes occurred, which still, to some extent, existed in the present patient, in spite of the great improvement which followed Professor Kocher's implantation of thyroid tissue into the medullary cavity of both tibiæ. The patient's thyroid symptoms seemed to have been at first of the nature of Graves's disease, and it was probably when the symptoms of Graves's disease had given way and become overshadowed by those of myxœdema that the main improvement in the sclerodactylia (which, however, as already stated, to some extent persisted—in a stage of contraction) set in.

Dr. GRAHAM LITTLE, in reply, said that he could not say what dose of thyroid she had been having, but he would try to find out. He would correct Dr. Parkes Weber and say that the symptoms of sclerodermia became pronounced only after 1908, whereas her first symptoms of Graves's disease, when Sir Thomas Barlow saw her, occurred in 1904. The sclerodermia became more obvious with transformation of the condition into myxœdema. The association seemed to be further corroborated by the fact that she improved on thyroid. In answer to the President, the vaccines were given for the pyorrhœa which she was suffering from, and which was supposed to explain the pernicious anæmia. There was no record of any blood examination, and there was no history of rheumatism.

Dr. E. G. GRAHAM LITTLE also showed a case of *general carcinomatous infiltration of the skin of arm (cancer en cuirasse), apparently resulting from an X-ray burn in treatment of an indolent breast scirrhus.* The patient was a single woman, now aged 52 years. There was no history of cancer or venereal disease in the family, the members of which were mostly long-lived. The earliest origin seemed to have dated from an injury to the left breast by striking it against a chest of drawers, after which accident a small nodule was noted in the breast in June, 1904, and some enlarged glands in the left axilla were first noticed in February, 1905, but may have existed earlier. The tumour in the breast increased very slowly in size during the next nine years until it reached the dimensions of half an orange, but there was no suppuration in it until October, 1913. There was very little pain, and only at rare intervals, until suppuration developed. She was taken to a London hospital and given X-ray treatment, the first application on May 26th, 1914, the last on August 24th, 1915, forty-four treatments having been given between these dates. Ulceration of the breast had been present seven months before the first application, and during the treatment the tumour lessened in size and the ulceration decreased until, just before the last treatment, it was confined to a narrow, hard ring with a white edge. The left arm had begun to swell a month before the last treatment, but not at all notably, and there was no pain in it. On August 24th the application of the rays appeared to have been made by a nurse, and a very severe burn resulted, a blister forming which covered the whole area between the base of the throat and the lower margin of the breast. The skin sloughed off this area, leaving a large raw surface which gradually healed except at the centre, which remained ulcerated over a circinate area about 4 in. in diameter. The breast tissue on the left side had entirely disappeared, and the ulcer was on the level of the chest-wall, and superficially resembled a Paget ulceration in the particular that there were islets of sound epidermis in the ulcerated area. The edge, however, was hard, and at the axillary border merged into a very hard glandular mass which filled the axilla. The whole of the left arm from shoulder to wrist was swollen, and the skin thickened and reddened, with a sensation to palpation like the rind of a very thick-skinned orange. The arm was painful and immobilised. There was a moderate degree of pitting on deep pressure, but the œdema accounted only for a minor portion of the general swelling. The infiltration had advanced very rapidly apparently since the burn took place, though some swelling was noticed, as had been said, a month before while under X-ray treatment. There had, during the last two months, been acute neuralgic pain in the arm which had prevented sleeping, and the patient had lost ground in consequence. Since August, 1914, she had had no treatment beyond the application of hydrogen peroxide, zinc sulphate, and other weak antiseptics.

The case presented points of special interest in the history of a remarkably slowly growing scirrhus with only very moderate glandular enlargement in the axilla during nine years, the apparent dispersion of the tumour and diminution of the ulceration under moderate X-raying, but at the same time an extension of superficial carcinomatous infiltration, and a very rapid acceleration of this infiltration of the skin and glands after the X-ray burn. A portion of the skin from the extreme limit of the ulcer nearest to the axilla had been histologically examined (the slide was brought to the meeting), and definite and deeply disseminated carcinomatous infiltration was demonstrated to be present. This sufficiently disposed of the suggestion that the edge was the edge of a healing X-ray burn, a suggestion which was further negatived by the carcinomatous infiltration of the arm. The exhibitor had felt obliged to take the most serious view of the case, and had recommended the removal of the breast, arm, and shoulder-blade, with evacuation of the axillary glands.

The excellent notes were largely due to the brother of the patient, who was chief dispenser to the Children's Hospital, Shadwell.

The PRESIDENT asked if there was any precancerous condition of the nature of Paget's disease. He feared the graver issue was likely to happen, and that the left arm was implicated in the disease. Amputation of it seemed to be indicated. He hoped they would have a later report on the case.

Dr. KNOWSLEY SIBLEY remarked that Dr. Little spoke of the very rapid extension of the carcinomatous growth. He did not know whether he considered that the whole of the ulceration which they saw was malignant; he did not think it was so; the edges were healing, and in many places there was a healthy granulating surface. Though she had had a severe X-ray burn, he was not clear that that had produced a rapid extension of the cancer, either from the history or the present appearance. The œdema of the arm was what generally happened in these advanced cases of breast cancer, and the patient said the arm swelling started three weeks before she received the burn. He understood that though the rays were given under the superintendence of a doctor at first, in the later stages a nurse alone did the administration. He did not know from what part of the disease the section was taken for microscopic examination.

Dr. Alfred Eddowes said that many years ago he used an old-fashioned remedy for the pain in hopeless cases of malignant disease—namely, the injection of a drop or two of solution of bromine in alcohol. It completely destroyed a large gland in the neck. So great was the relief due to sloughing and reduced pressure that the patient's friends even hoped for a cure, though he had explained previously to the operation that it could only relieve suffering.

Dr. Graham Little, in reply, said the section shown was taken from the outside edge, and that was where the scirrhus was definite. He regarded the swelling of the arm as more than œdema; it was undoubtedly an extension of the carcinomatous infiltration of the skin, and as the axilla was full of enlarged glands, he had suggested that amputation of the arm might be the best course.

· Dr. W. Knowsley Sibley showed a case for *diagnosis* (*tuberculosis*). The patient, D. W—, was a stout, healthy-looking, single woman, aged 23, who had five brothers and sisters, all well, and both parents were living. The father was stated to suffer from asthma and bronchitis. When a child, the patient had a large superficial ulceration over the right calf which had left a pale scar, and at about the same time she had an abscess over the region of the left hip. Six years ago the patient suffered from lupus of the left cheek, leg, and ankle, all of which healed up after two years' treatment, leaving marked scarring. She also had some ulceration on the mucous membrane of the left upper eyelid, which was treated with radium. Three years ago an ulcer appeared between the big and second toe on the left foot, followed by some small hard papules scattered over the dorsum of the foot. About this time the left leg swelled, and had remained considerably œdematous ever since. The surface of the leg up to the knee was cold, but there was no loss of sensation nor any pain or discomfort in walking. A verrucose condition existed in the region of the former ulcer between hallux and second toe, and there were several hard cutaneous nodules, the size of peas, scattered over the dorsum of this foot. The right leg was normal, and there were no obvious visceral lesions to be detected. The von Pirquet reaction was on two occasions distinctly positive, and the Wassermann negative. A section of one of the nodules from the foot showed the structure of a granuloma, with a tendency to giant cell formation.

The case was obviously one of tuberculosis, but he showed it in order to elicit opinions as to the nature of the œdema in the leg. He could not ascertain that there were any visceral lesions, and there was no albumin in the urine.

Dr. PRINGLE said that the condition of the leg was typical of that described in France many years ago as "tuberculous lymphangitis" with elephantiasis; there were models of several cases in the St. Louis Museum. The nodular lesions were, he had no doubt, lymphatic varices. An excellent case was described and illustrated by Mr. John Cahill in the *British Journal of Dermatology* in 1895,* which was annotated by himself. He was not aware of any histological reports on these cases, and therefore he did not know whether the name tuberculous lymphangitis was microscopically justified. His present impression was that cases of this sort, of lesser degree, were not very uncommon; he had had a considerable number under observation. The concomitant phenomena of tuberculosis were seldom so manifest as in Dr. Sibley's case, but their existence only bore out the general tenor of his remarks. His experience was that these cases did just as badly as did the analogous syphilitic elephantiasis.

Dr. F. PARKES WEBER said that as there were tuberculous lesions present, he supposed one must regard the case as one of "tuberculous lymphangitis," and commencing "tuberculous elephantiasis." But the difficulty was to be certain that, in addition to the local tuberculous lesions, there was not associated a condition of unilateral, persistent, so-called "idiopathic œdema" or "trophœdema" (which was an early stage of some cases of so-called "idiopathic elephantiasis"), independent of the tuberculous lesions in question. Such cases of "idiopathic œdema" in lower extremities might be unilateral or bilateral, and might extend upwards to the knee-joint or to the hip; they were more commonly met with in females than in males, and, as far as he knew, could not be permanently cured by any kind of treatment.

Dr. G. PERNET agreed with Dr. Pringle. He did not see that this condition had any relation to trophœdema or to idiopathic elephantiasis, whatever that might mean. This patient presented what was analogous to syphilitic elephantiasis.

Dr. EDDOWES had had the good fortune to be able to watch a similar kind of case for twenty-five years. Originally his patient had lupus on the end of the nose. By taking away a part of the nose he improved her personal appearance and the disease had not recurred. On the foot the first lesion, in addition to the swelling, was a warty condition between the great and second toes, and he thought that might be the original site of inoculation of tubercle in that leg. The leg became enormously swollen, but by treatment with mercurial ointment a wonderful recovery occurred, and the patient now considered herself well. He looked upon the prognosis in such cases as decidedly favourable. The particular patient referred to did not require any treatment now, and she was in regular employment. He recommended that in the present case 10 gr. of yellow oxide of mercury to the ounce of paraffin moll. be rubbed over the leg and between the toes, in order to maintain asepsis as well as the absorption of mercury.

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* *Brit. Journ. Derm.*, 1895, vii, p. 1.

Dr. SIBLEY, in reply, said this patient had been in bed six weeks, and the leg was now more swollen than at first. He did not apply radium; he had not seen her until quite recently.

Dr. S. E. DORE showed a case of *Dermatitis herpetiformis*. The patient was a rather tall and thin young man, aged 26 years, who was sent to him by Dr. Cumming Grant. His father died at the age of 30 years of inflammation of the lungs; his mother, aged 50 years, was alive and healthy. He had one sister, aged 29 years, who suffered from phthisis. His own health had been fairly good, but he had had three attacks of pleurisy, the last attack, five years ago, being followed by empyema. He was a journalist by occupation and of a somewhat nervous temperament. The skin disease began last April, ten months ago, and he first noticed a few slightly itchy spots on the shoulders and arms, which became much more numerous and spread over large areas of his body towards the end of the year. When he last saw him he presented a characteristic eruption of Dermatitis herpetiformis, with grouped papules and vesicles, but as the result of taking increasing doses of Fowler's solution since the beginning of January, the eruption had nearly disappeared, leaving only pigmentation and a few papulo-vesicles in the areas previously affected. To him the eruption was striking by reason of its almost perfect bilateral symmetry, which had not been a conspicuous feature in the cases he had previously had under his care. It affected the shoulders and posterior scapular regions, the centre of the back, lateral surfaces of chest, anterior and posterior surfaces of thighs, popliteal spaces, upper part of buttocks and intergluteal fold. The glands in the groin were enlarged, and the eruption gave rise to intense itching and burning, principally at night. He would be glad of suggestions for treatment other than that by arsenic.

The PRESIDENT presumed that the exhibitor did not consider that he had yet obtained the fullest benefit from arsenical treatment, and that he proposed to continue the administration until the lesions had disappeared. He asked if he had been able to detect evidence of intestinal toxæmia in the patient.

Dr. MACLEOD stated that salvarsan had been tried in these cases, but the results had been uncertain.

Dr. ADAMSON said that another treatment was the injection of human blood, which had been employed in cases of pemphigus and of Dermatitis herpetiformis. He had not yet used it for Dermatitis herpetiformis, but, with Dr.

Stansfeld. he employed it in five or six cases of pemphigus, and in two of them they got good results; in a third the patient was improving, though not so clearly, as the result of the injections. In the others there was practically no result. It was worth trying in a case of Dermatitis herpetiformis which did not yield to arsenic: 10 to 20 c.c. of blood from a healthy person was injected into the veins or the buttock of the patient, having first determined (for intravenous injection) that the two bloods were compatible, for it would not do to inject a blood which would hæmolyse the blood of the patient.

Dr. PRINGLE said this man represented a type of case with which he knew Dr. Dore was familiar, the "old-fashioned" type of Dühring's disease, which did yield with some amount of certainty to arsenic; it was a point made by Dühring in his earliest writings on the subject. But the quantity of arsenic administered must be ample; every patient appeared to have his own personal dose. Dr. Dore would remember a man who had numerous attacks, and they always yielded rapidly when they got his dosage up to 15 minims of liquor arsenicalis three times a day. Short of that quantity, the drug did not seem to influence the disease in the least. In such cases the drug had to be pushed up to or even somewhat beyond the physiological limit. It would be interesting to find out what doses of arsenic had been taken in this case. He thought that the disappearance of itching was often the first manifestation of recovery, either temporary or permanent.

Dr. H. G. ADAMSON showed a case of *Herpes recurrens of the right cheek in a boy, aged 9 years.* He had brought this case as a good example of that form of Herpes recurrens which attacked a large area of one cheek and which had been described particularly by Dubreuilh. It was an illustration of the fact that extensive herpes of one cheek was not necessarily Herpes zoster—*i.e.* herpes corresponding to the second division of the fifth nerve. In this boy the eruption had appeared several times a year since he was aged 1½ years, so that he had already had twenty-five to thirty attacks. He felt poorly before each attack, and had a rise of temperature (100° F. to 101° F.) during an attack, but there were no other symptoms. The eruption left no scar. He showed photographs of extensive recurrent herpes of the cheek, of the ear, of the gluteal region, of the wrist, and on one finger. The ætiology of these cases was obscure. Dr. Sequeira has suggested some local source of irritation which acted reflexly, such as adenoids in the facial cases. This boy had some adenoids which would be removed, and it would be interesting to see whether the eruption ceased as it did in one or more of Dr. Sequiera's cases, but it should be noted that recurrent herpes occurred with various febrile illnesses—pneumonia, diphtheria, scarlet fever, typhoid, etc., and in such instances reflex irritation did not seem to explain it.

Dr. **Graham Little** agreed with Dr. Adamson that this was Herpes simplex, and that that was a different condition from Herpes zoster. He was still an adherent of the view which Dr. Head expressed. He regarded a recent case of Mr. Trotter's as similar to this present case, and as an instance of Herpes simplex, in that, as Dr. Parkes Weber pointed out, there was no wasting of muscles, which would be present if it were a trophic nerve affection. There has been recently a little sporadic and not very authoritative literature as to the connections between Herpes zoster and Herpes simplex. A South African writer collected forty cases from the literature of apparent association either in families or schools, but there is always a difficulty about diagnosis. Since he went through this literature he had a curious case of severe zoster in the husband of a woman who had suffered from Herpes simplex for fifteen years; she had an attack once in ten days, during one of which the husband came out with severe Herpes zoster. Head's observation of maximal points of incidence in Herpes zoster was a valuable differentiation in some cases, and was never present in Herpes simplex.

Dr. **Adamson**, in reply, thought we might group herpes under three or four headings—namely: Herpes zoster, which was due to a specific micro-organism which attacks the posterior root ganglia and protects against a second attack; arsenical herpes; and herpes (which may be recurrent) due to pressure on a nerve. All these forms are associated with a definite nerve lesion. Herpes recurrens or Herpes febrilis, of which the real cause was obscure, belonged to a class apart, and was distinguished by recurrence of the attacks and by the fact that the eruption did not correspond with a unilateral nerve distribution.

Dr. J. M. H. **MacLeod** showed a case of *necrosis of the skin from handling "composition" (an explosive).* The patient, a woman, aged 30 years, a munition worker, had painful small necrotic lesions on the hands, especially the tips of fingers, which lasted about a fortnight. She attributed them to handling an explosive composition containing mercury, antimony, potassium, and sulphur, etc. The patient had also a slight iritis from the same cause. Several of the other workers in the same factory were similarly affected.

Dr. G. **Pernet** had had one or two instances in people employed in a similar way; they had come on account of various forms of dermatitis on the fingers and forearms. He would try to bring a case next time.

Dr. F. **Parkes Weber** asked if these lesions had been noticed only in cold weather. One knew how cold weather might intensify the harmful results of irritating antiseptics on the skin (as used, for instance, in the ordinary way for disinfecting the hands). Perforation of the nasal septum had been reported as a result of working with chromates or chromic acid.

Dr. **MacLeod**, in reply, said that the patient had to handle the highly explosive powder and to work it, with her fingers, into a paste with methylated spirit and press it into a mould. This procedure was probably the cause of the necrosis.

Dr. GEORGE PERNET showed a case of *multiple comedones of frontal region in a boy.* The patient was a boy, aged 8 years, with numerous small comedones about the upper part of the forehead, arranged transversely and impinging on the margin of the scalp. They had been present about two and a half months. There was no sign of inflammation or suppuration about the comedones. The mother had lately been rubbing in brillantine on account of a dry seborrhœa of the scalp. This, combined with rubbing of the cap, had no doubt given rise to the comedones. Although he had seen a number of children in his clinic, the condition was not a common one in his experience. Radcliffe-Crocker* was apparently the first to call attention to this class of case in infants and young children.

The PRESIDENT said that the point of interest was that the lesions did not undergo suppurative action. Such cases were seen here less frequently than formerly, probably for the reason that they were not uncommon.

Dr. PRINGLE thought the idea of a brillantine of sorts being responsible for this eruption was probably right: and he probably had used the same cap with the lining unchanged for a long time, which was a common cause of seborrhœic scalp trouble.

MEETING held on March 16th, 1916, Dr. J. H. STOWERS, President of the Section, in the chair.

Dr. J. M. H. MACLEOD showed a *case for diagnosis: Provisional diagnosis: Nodular Lupus erythematosus followed by atrophy of the skin and subcutaneous tissue.*

The patient was a short, spare woman, aged 48, who presented an irregular atrophic condition of the face affecting both cheeks, but most markedly so on the right side, producing pronounced disfigurement. The atrophy had resulted from the involution of pinkish nodules and plaques. On the right side of the face the skin was atrophic and irregularly depressed from the right malar prominence down to the angle of the jaw, while the malar region on the left side was similarly affected.

The general health and nutrition of the patient were good. In her childhood she had suffered from tuberculous glands in the neck and axilla on the right side, the scars of which were still noticeable, but she had no signs of active tuberculosis. There was a history of tubercle in the family, a sister having died of phthisis.

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* See his *Atlas*, plate lxxxiii, fig. 5.

She first came under the observation of the exhibitor at Charing Cross Hospital eight years ago, when she presented over the right malar prominence a reddish, slightly infiltrated plaque about the size of a penny with a well-defined irregular outline, the surface of which was smooth and covered with a network of dilated capillaries. On the left side of the forehead there was a small reddish nodule with a telangiectatic surface. The diagnosis then made was Lupus erythematosus of the nodular variety described by the late Dr. Radcliffe-Crocker.

The lesions were treated by zinc ionisation and disappeared after a few applications, being followed by atrophy involving not only the skin, but the underlying subcutaneous tissue. The atrophic skin had not the appearances usually associated with the scarring left by Lupus erythematosus; there were no follicular pits—indeed, some of the lanugo hairs had remained, and the surface of the skin was smooth and soft. It seemed as if the main part of the atrophy had taken place, not in the skin, but in the subcutaneous tissue immediately underlying it.

The diagnosis was exceptionally difficult, but nodular Lupus erythematosus seemed the most probable. The question of syphilis was eliminated by the whole facts of the case and the Wassermann reaction being negative. The behaviour of the lesions and the telangiectases differentiated it from the superficial type of Lupus vulgaris. It seemed as if the pathological process involved the corium and upper parts of the subcutaneous tissue. Unfortunately a microscopic examination had not so far been possible owing to difficulties in obtaining a biopsy.

Dr. KNOWSLEY SIBLEY asked whether sclerodermia would not cover the condition. This case reminded him of one he had a few years ago, almost identical in appearance. His patient, however, had the condition well developed when he saw her. She had marked atrophy on the left side only, which gave the impression that her malar process had been removed, but she had never had an operation. She had a punched-out ulcer in the margin of it which was obviously syphilitic. It healed up with antisyphilitic treatment. There had never been ulceration over the rest of the patch. The patch was not produced by ulceration, and as far as could be determined it was preceded by a rash, which had been scraped and X-rayed, after which, as the patient expressed it, "the tissues faded away." It was an asymmetrical case. He had a photograph of it, and the condition had been coming on for seven years when he first saw her.

Dr. F. PARKES WEBER ventured to suggest that this was a case of what he would like to call "double hemiatrophy" of the face, in which the cutaneous inflammatory disease described by Dr. MacLeod acted as an *exciting cause*. Traumatism was now generally admitted as a possible exciting cause of facial hemiatrophy, and one could therefore easily conceive that other lesions, such as inflammatory skin-diseases, might, in predisposed individuals, occasionally also act as exciting causes. Facial hemiatrophy was doubtless in some way allied to sclerodermia, for there were several cases known in which hemiatrophy of the face, or of the face and whole body, had been accompanied by sclerodermatous changes (not necessarily limited to the side of the hemiatrophy).

The PRESIDENT agreed with Dr. MacLeod's view of the case.

Dr. S. E. DORE understood that Dr. MacLeod diagnosed the precedent condition as Lupus erythematosus. He once had a somewhat similar case in a middle-aged woman in which treatment was followed by deep atrophy of the skin of the same type, and in which the diagnosis of "Lupus erythematosus nodularis" of Radcliffe-Crocker was made. He had seen cases in which a condition analogous to sclerodermia had followed Lupus erythematosus, but he did not think this case was of that kind.

Dr. G. PERNET did not remember ever seeing anything quite like this case. As Dr. MacLeod had been observing the case for eight years and was able to exclude morphœa and sclerodermia, he thought they could clearly exclude those conditions.

Dr. MACLEOD, in reply, said there had been no definite sclerodermia in this patient, but simply an atrophy following the removal of the indurated lesions by treatment in which the skin remained soft and pliable.

Dr. GEORGE PERNET showed a case of *staphylococcia in a xerodermatous patient*. The patient was a girl, aged 6 years, who first came under observation in November, 1915. She then presented multiple areas of closely aggregated pustules in foci and *en nappe*, which extended at the periphery and involved the scalp, face, neck, and limbs. The disease started at the age of two. Xerodermia was also present. There was inguinal and femoral adenitis.

In addition to local remedies, the treatment had consisted of vaccine injections of stock mixed staphylococcus, gradually increased from 1 million to 200 millions, and internally thyroid from the point of view of the xerodermia. The patient had improved considerably.

Although a case of this kind would be classed under the heading of eczema, he considered it came into the category of staphylococcia, and was related to the group of *Pyodermites en nappe et en foyers à progression excentrique* (of Hallopeau and others), to the condition he had described under the name of "Dermatitis pustulosa vegetans recurrens."* He had brought forward the case in order to hear the opinions of members of the Section.

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* Pernet. *Journ. of Cut. Dis., etc.*, New York, September, 1912.

Dr. S. E. **Dore** did not know why Dr. Pernet objected to the term "eczema" in this case. Xerodermatous subjects frequently suffered from eczema of the extremities, and the excessive vulnerability of their skins also made them liable to staphylococcus infection.

Dr. H. G. **Adamson** regarded this as a characteristic case of chronic eczema in a child. Most cases of chronic eczema in children dated from infancy, and began as the well-known infantile eczema of the face particularly. The majority of infantile eczemas got well at or before 2 years of age; but some continued into childhood, and patches occurred on the trunk and limbs. Such cases were most obstinate to treatment, because the eczema patches were kept up by constant scratching, and they often got lichenified and secondarily infected. Dr. Pernet's case seemed to him to be a typical eczema of this sort.

Dr. **Alfred Eddowes** had a case like this now under his care, and drew a very marked distinction between it and ordinary eczema in children. He thought the xerodermia played the most important part. Such children were delicate, and needed building up in every way. He labelled his case Impetiginous eczema. superadded upon xerodermia. No doubt there was infection, but the best treatment was to give thyroid, phosphates, and cod-liver oil, in addition to local measures. Some patches became thick and irritable, and caused bad nights. He had found X-rays of great benefit to these patches.

Dr. **Pernet**, in reply, said that he did not agree from the clinical point of view that the case was one of advanced eczema. It began as a staphylococcia. The xerodermia was an additional factor. As a result of treatment, the case was very different from what it was when originally seen.

Dr. **George Pernet** showed a case of *primary syphilitic chancre of the lip*. The patient was a widow, aged 32 years, who was first seen on March 10th, 1916, for a sore on the lower lip to the right of the middle line, of one month's duration. It had resisted ordinary treatment, and had become gradually larger and harder—the usual history, by the way. The sore was a typical primary syphilitic chancre. The submaxillary glands were greatly enlarged, and there was also submental adenitis. There was post-sternomastoid and inguinal adenitis, and a typical mottled roseolar rash about the body and limbs. The patient complained of bad nocturnal headaches. Nothing had been found about the vulva. Galyl 0·20 grm. had been given intravenously on March 11th, 1916, and followed up by mercury (a calomel cream) locally.

Captain C. H. **Mills** said that in most of the text-books on syphilis one found it stated (as a point in the differential diagnosis) that primary sores of the lip were more common on the upper lip, whilst epithelioma was more often seen on the lower lip. But most of the cases of labial chancre he had seen had been on the lower lip (as in this one), and he considered, therefore, that the situation was of no diagnostic importance.

Dr. Pernet, in reply, said that his experience led him to agree with Captain Mills—the labial chancres he had seen had more frequently been on the lower lip.

Dr. E. G. Graham Little showed a case of *chronic diffuse papillomatosis of the left foot and leg.* The patient was a married woman, aged 52 years, separated from her husband. She gave no history of syphilis, and the Wassermann reaction was negative. Her left eye was removed by his colleague, Mr. Paton, in 1907, and his report stated that the eye was taken out for a "perforating hypopyon ulcer, of pneumococcal causation. There was no evidence of syphilis." The patient first came under his care in January of this year, and then gave a history of having had the condition of the foot for about a twelvemonth or longer. She seemed to have had some septic infection of the leg prior to this, whether an abscess or a varicose ulceration it was difficult to determine. The left leg was reddened and swollen, with a brawny œdema, such as was common in varicose ulcer. The lower third of the leg and the whole dorsum of the foot were covered with a thick carapace-like warty envelope; the surface was rugose and dry, and innumerable closely juxtaposed small warts occupy the affected area. There was some blackening of the skin in these parts, probably due to external dirt. The skin was inelastic and stiff, and the sole, though free of warts, was hard and hyperkeratosic. The right foot was somewhat swollen, and the skin covering it was hardened and hyperkeratosic, but to a much less degree. There was no papillomatosis here. The patient was sallow and thin and had lost much flesh in the last ten years. But there was no pigmentation and the mucous membranes were unaffected.

He regarded the case at first as an eczematous hyperkeratosis, started by a varicose ulcer, and this view was supported by the presence of a copious discharge, which speedily dried up with application of ung. acid. salicyl. and oil of cade. A section of the skin was obtained, and on examination of this he was somewhat struck with the similarity to sections of a case of Ancanthosis nigricans which he had reported.* The section shows a pure papillomatosis, with great increase in the thickness of the stratum corneum (the section was taken from the upper margin of the carapace, on the leg) and of the stratum granulosum, with a certain degree of a mononuclear cellular infiltration of the papillary zone of the corium, but there were no cellular foci suggestive of tuberculosis, and this finding seemed to negative an alternative diagnosis of which he had thought—namely, a "verrucose tuberculosis, with elephantiasis." The absence of pigmentation militated, of course, against the diagnosis of Acanthosis nigricans, but there were some instances of this rare disease in which pigmentation was later in development than the papillomatosis. The absence of fœtor, or any but the most moderate degree of sepsis during his observation of the case, did not dispose him to regard the case as a septic papillomatosis, nor was he familiar with this degree of involvement in any locally septic conditions. He was, however, very open to suggestions of this causation.

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* *Brit. Journ. Derm.*, 1901, xiii, p. 42; 1902, xiv, p. 26.

Dr. MacLeod said that in his opinion the condition was probably of septic origin. For comparison with it he showed a coloured drawing of a case of "Elephantiasis nostras," which was under his care at Charing Cross Hospital, in which the foot and ankle were similarly affected. It occurred in a middle-aged stout woman, with varicose veins, and followed on ulcer in the leg. In this case there were recurrent attacks of lymphangitis.

Dr. Pernet was familiar with this sort of case, but during the last few years he thought there had been fewer of them in hospital work. He regarded them as elephantiasis with staphylococcic infection, leading to the warty growth. In tropical medicine these feet have been called "mossy feet." He did not see any connection between this condition and Acanthosis nigricans.

The President considered that the case was of septic origin.

Dr. S. E. Dore said that it was important to remember that the patient had suffered from varicose veins for many years, and he thought such a condition could follow chronic venous congestions, to which a septic element was possibly superadded.

Dr. H. G. Adamson agreed with Dr. Pernet, that it was a familiar form of warty growth or "mossy foot" associated with elephantiasis; they might see it with any form of elephantiasis. The diagnosis rested between tuberculous, syphilitic, or recurrent streptococcal infection. In this case he thought it might be syphilitic. There were nodules on the upper part of the leg, and the scars rather suggested syphilis. Had there been any antisyphilitic treatment?

Mr. McDonagh said that when he first saw the case the diagnosis of syphilis entered his mind, but he was aware that septic trouble and tuberculosis might give rise to a similar condition. The microscopical section would fit in with any one of these three causes. To establish a correct diagnosis it would be necessary to undertake further tests.

Major Gray thought that the history in this case seemed to suggest tuberculosis or septic infection rather than syphilis, because, as far as he could make out, the condition began with definite abscesses along the lymphatic tracts There was one abscess over the internal malleolus, and another on the inner part of the thigh, both of which burst and discharged for a time. The present lesion apparently started from the abscess in the foot.

Captain C. H. MILLS asked if the technique of the Wassermann test employed in this case was the original technique, or a modification, in view of the fact that this patient had had three miscarriages, and that the scarring higher up the calf was very suggestive of previous gummatous ulceration, he thought it might be well to administer a provocative injection of salvarsan, and twenty-four hours later do another Wassermann test, this time using the original method.

Dr. GRAHAM LITTLE, in reply, said the Wassermann test in this case was performed by Dr. Alexander Fleming, who no doubt used his own modification of the original Wassermann test.

Dr. ALFRED EDDOWES showed a case of *acute Lupus erythematosus, with nodular necrotic cutaneous tuberculides of arms and hands, feet and legs.* The patient, a strong, well-developed woman, aged 27 years, with a good family history, was seized at the end of December last with great and sudden swelling of the face, and at the same time observed spots on her arms. Lately the swelling of the face had become less, but nodules have been noticed on the feet and legs.

Dr. G. PERNET considered this was a case of acute Lupus erythematosus d'emblée, in which there was no albuminuria. He collected the records of nine cases in addition to his own, and only one out of the ten patients survived, notwithstanding various methods of treatment.* The small lesions on the arms and backs of the hands came into the clinical picture of Lupus erythematosus of the acute type. There was an acute onset, with swelling of the face, and he thought that was very characteristic. Kaposi gave the name of Erysipelas perstans faciei to the condition, though it had nothing to do with true erysipelas. The case which survived did well on quinine, and a recurrence again yielded to the drug. He thought it should be tried in this case. Dr. Payne, of St. Thomas's Hospital, introduced quinine in the treatment of Lupus erythematosus. He asked if there was albuminuria in this case. There was no albuminuria in the ten cases he referred to. The Lupus erythematosus cases with albuminuria were in a different category.

The PRESIDENT asked if the exhibitor regarded the eruption on the face as of the same nature as that on the extremities—*i.e.* were they both, in his opinion, of tuberculous origin.

Dr. DUDLEY CORBETT asked what was the state of the mouth for which Dr. Eddowes placed the patient in the dentist's hands. As far as he could see there was a considerable amount of pyorrhœa present which might be a contributory factor in the case.

Dr. H. G. ADAMSON thought it was acute Lupus erythematosus. He did not see any reason for calling the arm lesions tuberculides, and they were not necrotic. He did not think there was much evidence that acute Lupus erythematosus was tuberculous. The fatal cases he had seen died of pneumonia. He asked Dr. Pernet what were the causes of death in the nine cases he collected.

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* Pernet, *Le Lupus érythémateux aigu d'emblée*, Paris, 1908.

He thought the only treatment for acute Lupus erythematosus was to keep the patient strictly in bed. He had seen cases get well when they had been kept in bed.

Dr. **Pernet** said his patient with acute Lupus erythematosus d'emblée had died of pneumonia, which was also the cause in some of the other cases he collected. In his monograph on those cases he said he could not put his finger on tuberculosis as the essential cause. He agreed that an important indication in these cases was to keep the patient in bed; he assumed that that had been done.

Major **Gray** said that some members might remember a case which he showed a little while ago.* It was extremely acute, many of the lesions actually having hæmorrhagic bullæ. Whilst that patient was under his observation, a period of about eighteen months, he thought she had three attacks, the condition clearing up in the intervals between the attacks. The second was the most acute, and was complicated by pneumonia, from which she recovered. A slight pleurisy occurred in the third attack, which was milder. He did not remember what medicinal treatment was given, but he remembered she was kept in bed.

Dr. **Eddowes**, in reply, said the lesions were both atrophic and necrotic. In answer to the President, whether "tuberculide" or not, he considered these nodules were the isolated lesions of erythematous lupus. As the patient had some bad teeth, he passed her on to the dentist. He had not found any lesions of the disease in the mouth. She was getting better without rest in bed. Twenty years ago he stated that the nodular necrotic cutaneous tuberculide—then often called folliclis—was in reality a well-marked isolated lesion of Lupus erythematosus, but his view was rejected by several of the leading authorities, and he did not receive any articulate support. Nevertheless he had stuck to his point and reasserted the statement with confidence, although the writers of text-books did not see it yet. A question that awaited an answer was if this eruption was due to tubercle in the system, why did they not see it oftener in cases of acute general tuberculosis. He might be asked if he was right in considering that these nodules were the same as Lupus erythematosus, why did the face often escape when the nodules appear profusely over the limbs. His working theory was that the disease attacked the face especially and left scars behind because of pre- or co-existing seborrhœa and acne, or both. We had an analogy in lung abscess from tubercle—a double infection.

Dr. H. **Spence** showed a *recurrent syphilide simulating reinfection.* The patient was a male, aged 31 years. He first noticed the primary lesion on the under surface of the penis about May 20th, 1915, being six weeks after exposure. Upon his first attendance at the hospital three weeks later he exhibited an indurated sore somewhat larger than a sixpenny piece, and associated glandular enlargement of the specific type. He received four intravenous injections of "606," and left the wards on July 10th, attending the out-patient clinic ten days thereafter, when he received an intramuscular injection of mercury, and the chancre was found to have healed. His work then necessitating his removal from London, no further treatment was taken, and for several months he was without symptoms. Early in January last he noticed a small spot to one side of and distinct from the original sore, which he stated healed in a week's time, to be immediately succeeded by the two larger sores now in evidence, one upon the same site as the place just referred to, the other approaching the upper surface of the penis. At the same time there also appeared the rounded sore on the left fronto-parietal region, nearly the size of a shilling, and similar ones on the dorsum of the tongue and in the left groin, as well as smaller lesions on the upper lip (1), scalp (2), chest (1), left leg (1), and back (6). There was also a distinct induration under the foreskin. A scar marked the site of the original sore.

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* *Proc. Roy. Soc. Med.*, 1914, vii (Derm. Sect.), pp. 82–84.

Captain Mills asked if the chief point of interest was that these lesions were supposed to resemble primary chancre. [Dr. Spence answered in the affirmative.] It did not occur to him that any one of them resembled a primary sore. That on the left frontal region started as a periostitis, which, subsequently involving subcutaneous tissues and skin, then broke down. He had not probed it, but he thought bare bone would be found there. A gumma was developing at the point of pressure where the man wore his truss; there were others on the shoulder corresponding with the pressure of his braces. He did not think the tongue lesion resembled a primary sore of the tongue. There was no loss of tissue on the surface, and no actual ulcer. And he also regarded the non-indurated sore on the penis as gummatous.

The President said it was common experience in practice to see delayed results from good and appropriate treatment insufficiently administered, and it was likely that this was an instance of the kind. A continuous administration of the same remedies would undoubtedly cure the patient.

Mr. J. McDonagh said that this case was especially interesting for several reasons. The initial lesion was a large ulcerative chancre, a type of sore which was often accompanied by no enlargement of the inguinal lymphatic glands and by delayed secondary symptoms. In other words, the call for the production of resisting bodies was minimal; treatment with "606" rendered them still less necessary, with the result that when symptoms reappeared they aped the initial lesion, as they were to all intents and purposes developing on a new soil. The present type of sore on both the tongue and the penis was typical of a chancre, the characters of the latter exactly simulating the initial lesion. Had the initial lesion left no scar, and had not other sores appeared elsewhere than on the penis simultaneously, the case might easily have been diagnosed as one of true reinfection. In his opinion a large percentage of the reported cases of reinfection were really of the nature of the case here presented. In scanning the literature of syphilis, it was to be noticed that the reported cases of reinfection diminished year by year, and yet their treatment of syphilis was continually improving, a paradox which supported the view just enunciated.

Dr. **Pernet** said that although the sore on the penis might at first sight look something like a primary sore, he did not consider the appearances of the tongue were those of a primary chancre.

Dr. J. L. **Bunch** showed a case of *diffuse sclerodermia with sclerodactylia.* The patient, a woman, aged 50 years, had suffered from a gradually progressive sclerodermia for many years. The skin was now extensively involved and in many places had become hard, shiny, leathery to the touch, and rigid. In some places it was pigmented. In the upper limbs especially the underlying muscles had become atrophic. The sweat secretion of the involved areas was greatly diminished. The fingers were bent, fixed, and practically ankylosed. There appeared to be but little diminution of sensibility in the affected areas, and the occasional co-existing symptoms of cyanosis or quasi-Raynaud's disease (described by Chauffard and others) were not present in this case.

He brought the case in order to ask for suggestions as to treatment, and in relation to the case Dr. Graham Little showed at the last meeting, in which thyroid was implanted into the tibia of a patient suffering from sclerodermia with apparently excellent results so far as the sclerodermia was concerned. He wondered whether the same thing should be done in this case. The disease was spreading rapidly, and it only dated back fifteen months. She had been given thyroid by the mouth during the short time she had been under his care, but that did not appear to have caused any appreciable improvement. She had not yet had light treatment, as she had been under his care only a short time. He proposed to give her vapour baths, but he did not suppose they would arrest the disease.

The **President** asked if there had been any injury to the nervous system or nerve shock. He did not know whether any member would be willing to undertake implantation of thyroid in such a case. It was a complicated and serious method of treatment.

Dr. **Graham Little** said that this patient was under his care for several months, and for some weeks was an in-patient in St. Mary's Hospital, where she was treated with administration of thyroid extract by the mouth, and by massage, warmth and rest in bed. The condition, he was afraid, was stationary, and he was obliged to replace her by more urgent cases. With regard to the relative advantages of administration of thyroid by the mouth and by implantation, he noticed with some interest that Professor Starling, in the last edition of his *Physiology*, remarked that implantation offered no superiority over feeding by the mouth. In the case shown by him to which reference had been made, the lady was certainly greatly impressed by the effect of the two operations performed on her by Kocher, and he might have laid, perhaps, too much stress on these in the presentation of the case, for it must not be overlooked that she had throughout, in addition to the implantations, both before and after these, continuous feeding by thyroid, and that when she presented herself for a third operation Kocher refused to operate, and contented himself with continuing the oral administration of thyroid.

Dr. F. Parkes Weber understood that treatment by implantation of thyroid gland into the medullary cavity of long bones had never yet been carried out with the object of curing sclerodermia or sclerodactylia; for in Dr. Little's patient it was carried out against the thyroid disease, not against the sclerodactylia. If Dr. Bunch were to adopt the implantation method in this case, it would be therefore probably the first case in which such operative treatment had been undertaken to oppose sclerodactylia; though, as was well known, thyroid feeding, iodothyrine, etc., had been tried in the various forms of sclerodermia, not always, however, with beneficial results.

Dr. Pernet did not consider that large doses of thyroid should be given to a woman of this age, and the fact that she had got rapidly worse might be due to the thyroid administration having been pushed. He thought small doses should be given to patients of this age—large doses, it seemed, had a tendency to break such patients up.

Major Gray said there was one indication in favour of implantation of thyroid as against oral treatment, which Dr. Graham Little did not mention; he was speaking of thyroid treatment generally and not specially in scleodermia. A certain number of people could not take thyroid by the mouth without feeling ill. He knew of one case of myxœdema in which that was true, and implantation produced a distinctly good result, though only of temporary duration. A second implantation was done, with equally good temporary result. The implantation was into the abdominal wall.

Dr. Bunch (in reply) said there was a story of a fall three years ago, but this trouble did not date back as far as that. He did not think they could make the excessive dosing with thyroid responsible for the rapid advance in this case. He did not know that the patient had had any at all during the last six months until the last week or two. He was much struck with Dr. Little's recent case, and, perhaps, from what was now said, he credited the implantation with more good result than he should have done, as he did not know what, if any, additional treatment the patient had had.

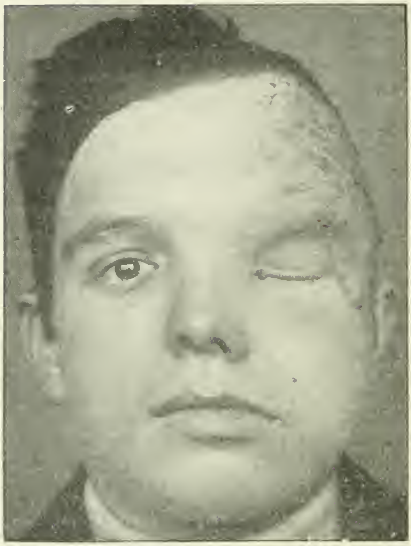
Dr. H. G. Adamson showed *sections from case of syringoma* (?) for Dr. Norman Paul, of Sydney.

A description of this case, with remarks by Dr. Adamson, appears on p. 106.

Dr. E. G. Graham Little showed specimens of *very unusual tumours of the skin.* The patient was not shown, as the operation for removal of the tumours was too recent to bring her from St. Mary's Hospital.

She was aged 22 years, a single woman, a "stiffener" by trade, and was first seen by him in December, 1915, when she showed him two swellings in the thickness of the skin, one in the left labium majus and one on the right forearm. The tumours were of stony hardness, deeply situated, about the size of a shilling and of a half-crown respectively, the smaller one being on the forearm; and the history was that they had been present for about nine months. They apparently caused no pain. The Wassermann reaction was negative, and the patient was a *virgo intacta*. His clinical diagnosis was fibrosarcoma, and at his suggestion the tumours were freely removed by his colleague, Mr. Ernest Lane, and he showed the pathological specimen together with a microscopical slide from one of them. Naked-eye inspection of the specimen shows a glistening-white infiltration of the tissues immediately below the integument for the depth of about ¾ in. Microscopical examination shows a slight acanthosis, and a dense and deep infiltration of the skin and subcutaneous tissue to the boundary of the subcutaneous fat, with a very extraordinary type of cell. There was a greatly swollen body with a very granular endoplasm, with numerous nuclei and an ill-defined wall. Masses of such cells were wedged together and contained by fibrous trabeculæ. Dr. Adamson, who examined the section, remarked on the resemblance of the cell to the so-called "xanthoma cell," and the resemblance was, in fact, close, but the clinical diagnosis of xanthoma was in no way suggested. Dr. Kettle, pathologist to St. Mary's Hospital, who had a unique experience of tumours, had not met with any quite similar condition, and the diagnosis remained at present obscure.

The illustration on the next page shows the result of Mr. H. S. Souttar's operation on the case of Dermatolysis and Molluscum fibrosum with congenital morbus cordis and kyphosis shown by Dr. J. H. Sequeira at the January meeting, and reported on p. 69. The orbit was cleared out and the upper part of the growth removed, the dependent skin being brought up, with an admirable cosmetic result. The tumour consisted of fibrous tissue and fat; there was no plexiform neuroma.



Dr. J. H. Sequeira's case of Dermatolysis after treatment (*see* page 147).

CURRENT LITERATURE.

OCCUPATIONAL DERMATOSES.

THE PREVENTION, SYMPTOMS, AND TREATMENT OF TETRYL DERMATITIS. Enid Smith, M.B., B.S. (*Brit. Med. Journ.*, April 29th, 1916.)

The writer acted as medical officer to munition works employing about 250 women where tetryl (tetra-nitro-methyl-anilin) is used. The hands of all workers, and in most cases the faces and hair, are stained yellow. The conjunctivæ and covered parts of the body are never stained, but the feet may be affected. Almost all workers suffer from dermatitis, which consists in its mildest form of irritation and roughening of the exposed skin. More serious cases show a papular eruption, and in the most severe cases there is acute œdema of the whole face; any variety of eczematous eruption may be seen. The attack may occur at any time, but usually after a fortnight's exposure. Conjunctivitis may occur with or without dermatitis. Nasal irritation manifests itself in excessive sneezing, and in epistaxis, but is never so severe as to keep a worker at home. Pharyngeal irritation has occurred in a few cases, and asthmatic attacks compelled two workers to leave. Constitutional symptoms are almost absent, but slight insomnia and "biliousness" have been noticed. If the symptoms are slight, the worker is encouraged to remain at work. If there is severe dermatitis, steaming the face with the subsequent application of wet cloths reduces the swelling and irritation. Calamine lotion, or equal parts of zinc ointment, lanoline, and castor oil, are afterwards applied. Lead lotion should be avoided on account of its dangerous affinity for tetryl. For conjunctival irritation colloidal silver acts well, and liquid paraffin is useful to allay nasal irritation. Suitable measures are taken with regard to the selection of workers and prophylaxis. S. E. D.

TROPICAL DISEASES.

DERMATITIS CUPOLIFORMIS. Aldo Castellani, M.D. (*Journ. Trop. Med. & Hyg.*, 1916, xix, p. 41.)

Under the heading of Dermatitis cupoliformis or tropical ecthyma, Castellani has described a peculiar nodular ulcerative condition of the skin met with in Ceylon, chiefly among Europeans. The lesions consist of dusky red spots which become raised and infiltrated, and gradually increase till they reach the size of a pea or a small cherry. After a time the centre of the nodule breaks down and an ulcer forms with a reddish fundus and often undermined edges. The lesions are usually situated on the feet or legs. They are peculiarly indolent, spontaneous cure seldom taking place in less than ten or twelve months. On superficial examination they are liable to be mistaken for Oriental sore, but Leishman bodies are absent.

From the lesions a streptococcus was isolated which is Gram-positive and does not liquefy gelatine. This streptococcus was named *Streptococcus tropicalis*. The condition can be experimentally reproduced by inoculating pure cultures of the germ into the hair follicles.

The most satisfactory treatment is the use of an autogenous vaccine, by which a cure may be effected in from two to three weeks. J. M. H. M.

NOTES ON THE SUCCESSFUL TREATMENT OF ULCERATIVE GRANULOMA PUDENDI BY MEANS OF TARTAR EMETIC. A. Breinl, M.D., and H. Priestley, M.D., Ch.M.(Syd.) (*Medical Journal of Australia*, March 18th, 1916. p. 237.)

Ulcerative granuloma is prevalent amongst the aborigines of North Queensland and the Northern territory, and occurs to a greater extent still amongst the natives of Western Australia. Until recently the treatment has generally proved difficult and unsatisfactory. The application of fuming nitric acid and other caustics to the granulating surfaces invariably gave rise to extensive cicatrisation, and, except in early cases, was seldom effective. Complete excision of the granulomata proved, even in early cases, difficult, and recurrences were frequent, even after prolonged periods of apparent cure. Advanced cases can be treated neither with caustics nor by excision, since the lesion nearly always spreads into the vagina and rectum, and extensive strictures would result from the latter treatment; late cases were, therefore, up to recently, incurable, and the patients died a miserable death.

Mercury and soamin in the hands of the writers and salvarsan in the hands of others have proved ineffective, as far as the actual lesions are concerned, but have led to considerable improvement in the general health.

X-ray treatment proved unsuccessful in two advanced cases under the writers' care. After the application of the rays the surfaces of the lesions began to heal and cicatrisation had apparently set in, but the diseased relapsed.

Tartar emetic as a parasiticide was introduced by Plimmer and Thomson for the treatment of trypanosomiasis in 1907. Gaspar Vianna (1913) used tartar emetic intravenously in dermal Leishmaniasis, and it has since been administered in kala-azar by Di-Christina and Caronia and Rogers. Aragao and Vianna (1913) published an account of the excellent results obtained from the use of intravenous injections of tartar emetic in ulcerative granuloma cases.

A Queensland aboriginal girl, about twenty years of age, suffering from extensive ulcerative granuloma, was admitted to the hospital. No definite history as to the duration of the disease could be obtained, but by all appearances she had been suffering for a number of years. The examination showed that the whole external genitalia were involved in the granulomatous process, and that it had spread into the vagina and along the perineum into the rectum.

The patient was kept under observation for five weeks and general hygienic measures only employed, in order to gauge the rate of spread of the disease. In spite of frequent antiseptic douches and strictest cleanliness the ulcerating surfaces did not show any sign of healing, but continued to exude a copious, fœtid discharge, proving that there was no tendency towards spontaneous improvement. The diagnosis was beyond doubt, since the regional lymph glands were not enlarged, and the characteristic Donovan bodies were found in great numbers in the discharge and in scrapings from the sore.

The Donovan bodies of ulcerative granuloma, named Calymma bacteria by the Brazilian observers, differ from the Leishman-Donovan bodies of kala-azar and Oriental sore. When mature they resemble in appearance large capsulated cocci, are oval in shape, and possess a single nucleus and usually occur intracellularly. In their earlier phases they are in more than one respect similar to the earlier developmental stages of Chlamydozoa, as they form zooglœa-like masses within the cytoplasm of endothelial cells.

The drug was administered in the way advocated by the South American observers. For the first injection, 0·06 grm. of tartar emetic was dissolved in 30 c.cm. of sterile saline solution, and injected intravenously by means of a large hypodermic needle attached to a funnel and tube. A small amount of normal saline was injected first, in order to make certain that the needle had penetrated into the vein, and was followed by the tartar emetic solution, and then by saline again, in order to prevent any antimony solution from entering the tissue at the site of injection. For the second injection 0·08 grm., and for the third and following 0·1 grm. was used. In this way seven injections were given in seventeen days, and, in all, 0·64 grm. of tartar emetic was administered. It was, unfortunately, practically impossible to continue the intravenous injections. After the seventh injection, in spite of comparatively extensive dissection, no superficial vein of the arm, large enough to allow of the free flow of fluid, could be found. It was, therefore, decided to administer the drug per rectum, since subcutaneous or intramuscular injections nearly always lead to extensive abscess formation. The rectum was thoroughly washed out with water, then a high rectal enema of 50 c.cm. of saline containing 0·2 grm. of tartar emetic was administered. These injections were well borne, readily retained, and did not give rise to any irritation. In this way nine injections were given in the course of twenty-one days.

The first three intravenous injections caused vomiting, which set in soon after the solution began to enter the vein; it was not severe, and ceased within a few hours. The subsequent injections, however, did not cause any inconvenience.

The effect of the injections was remarkable. The secretion from the granulomata increased considerably, but the fœtid odour became less pronounced and the patient complained of itching in the affected parts. After the second injection a distinct improvement set in, the edges of the sores began to cicatrise, and, after two weeks, the whole granulating surface was covered by a soft, whitish, epithelial layer, except at the upper part of the right labium minus, where a piece of tissue had previously been removed for microscopic examination. This small area was the last to heal, showing thus that tartar emetic had acted as a specific remedy.

The treatment has resulted in a temporary cure at least, and the patient was able to leave the hospital fourteen days after the last injection. Only observation over a more prolonged period will prove whether the cure was complete.

While recognising that definite conclusions as to the value of the drug cannot be obtained from this case, the success in this instance entirely confirms the observation of Aragao and Vianna, and justifies the recommendation of a further trial of this drug for the treatment of ulcerative granuloma.

J. H. S.

FUNGUS INFECTIONS.

THE OCCURRENCE OF RINGWORM OF THE SCALP IN SYDNEY. Norman Paul, M.B., Ch.M. (*Medical Journal of Australia*, March 18th, 1916, p. 237.)

Dr. Paul made microscopical and cultural examinations of thirty-four cases of scalp ringworm. The proportion of the different types was as follows:

Microsporons	14
Endothrix trichophytons . . .	19
Ectothrix trichophytons . . .	1

The microsporons were the Microsporon Audouinii, Microsporon lanosum, and Microsporon felineum.

Of the Ectothrix cases Trichophyton crateriforme was the commonest, cultures being of primrose colour. Tricophyton acuminatum occurred in several cases. Trichophyton violaceum was not observed.

The majority of the Endothrix cases were seen in private practice. There were two cases of Endothrix fungus in adults.

The variation in the relative frequency of ringworm fungi in different countries is well known, and Dr. Norman Paul's figures are useful in showing the fungi most common in Sydney. They more nearly approach the figures of Sabouraud in the Paris clinics than those observed in this country. J. H. S.

CONGENITAL CONDITIONS.

TELANGIECTASIA HEREDITARIA HÆMORRHAGICA (OSLER) E. Gjessing. (*Hospitalstidende*, November 10th–17th, 1915.)

Three cases are reported, a father and his two children.

Case I, aged 51 years, had had since childhood severe attacks of epistaxis which had become more frequent in late years, and also spontaneous bleeding from the lesions on the face and inside the mouth. The telangiectatic vessels had first been noticed on the face and buccal mucous membrane towards the end of "the twenties" and had continued to appear since that time. The skin lesions on the face, neck, and ears, consisting of spider nævi and dilated venules, were most numerous on the cheeks and auricles, while angiomata of about the size of a pin's head were present on the nose, tip and back of the tongue, with somewhat larger similar lesions on the hard palate, and also one single angioma on the conjunctiva of the right lower eyelid. No definite angiomata inside the nose. Smaller punctate telangiectases were also observed beneath two finger nails and on the dorsal and palmar surfaces of the fingers. Never any hæmaturia, purpura, nor melæna. No history of hæmophilia. Blood-pressure 177; interstitial nephritis, with granular casts in the urine, and some slight secondary anæmia. His mother and her two brothers had suffered considerably from nose bleeding, but so far as he knew these relatives had had no multiple telangiectases.

Case II, aged 30 years, son of Case I, showed severe anæmia and morbus cordis. Since childhood he had suffered much from epistaxis, which had been particularly severe during the later years. On the face were a half score angiomata, with a few similar lesions on the tongue and hard palate. Inside the nose were dilated vessels on the right side of the septum.

Case III, aged 25 years, daughter of Case I, was very anæmic. Since childhood she had had frequent attacks of nose bleeding, which still continued. On the cheeks during the last two years had appeared four to five small angiomata; the mucous membranes remained free.

Reference is made to eighteen other families occurring in the literature, the writer stating that his series is the first to be recorded in Scandinavian medical literature. He considers the hereditary disposition towards the development of multiple telangiectases to be of a degenerative nature, in which toxic factors, especially alcohol, may play an important part. A description of the microscopical appearance of the lesions is given, and mention is made of some other conditions which are accompanied by telangiectases. W. J. O.

NEW GROWTHS.

THE USE OF MERCURY IN VERRUCÆ PLANÆ JUVENILES.

C. J. White. (*Journ. Cut. Dis.*, 1916, xxxiv, p. 361.)

The writer reports a further series of juvenile flat warts treated by the internal administration of mercury. In a previous communication seven cases were reported with only one failure, in this contribution four more cases are recorded three of which were complete successes. The mercury was administered in the form of a pill of green iodide of mercury, one-eighth to one-quarter of a grain three times a day. J. M. H. M.

PATHOLOGY.

ANAPHYLAXIS IN ECZEMA (A Preliminary Report). C. J. White. (*Journ. Cut. Dis.*, 1916, xxxiv, p. 57.)

According to the writer, eczematous infants usually present in their stools an excess either of fat or of starch. An excess of the former element usually means a moist eczema, and of the latter a dry type. If the amount of fat or of sugar from the milk be reduced, it is claimed that a decided amelioration of symptoms takes place. When eczema is present and neither fat nor starch appear in excessive amount in the fæces, it is recommended that the skin should be tested with regard to its susceptibility to other articles of diet such as egg, butter, etc. This is done by a procedure somewhat analogous to the von Pirquet test for tuberculosis, the method being as follows: The upper layers of the epidermis on the flexor surfaces of the forearm are abraded in eight places in two parallel rows of four by the rotation of a dental burr, neither blood nor serum being drawn. On the first abrasion is placed a drop of fat-free milk, on the second a drop of egg albumin, on the third a small piece of salt-free butter, and on the fourth a few grains of lactose or a drop of oatmeal water. On the parallel controls nothing is used. Simply breaking the surface of the epidermis in this way seems to produce no reaction, but after the food-stuffs have been applied there is a slow and gradual change if the tests are positive, the acme of reaction occurring in about thirty minutes. The maximum result observed has been a pink-red elevated papule, never a wheal or a vesicle. All degrees of reaction up to this maximum have been noted from a simple erythema.

This cutaneous method can be extended to the study of other food elements in eczematous patients. Normal people, so far as was ascertained, do not react to these tests, but individuals suffering from chronic eczema seem to exhibit anaphylactic reactions to one or more types of food substances, and when these are eliminated from the diet improvement may be expected. J. M. H. M.

ERYTHEMATOUS AND URTICARIAL ERUPTIONS RESULTING FROM SENSITISATION TO CERTAIN FOODS.

W. L. McBride and E. H. Schorer. (*Journ. Cut. Dis.*, 1916, xxxiv, p. 70.)

The conclusions arrived at in this paper are as follows: Certain of the protein foods on ingestion by certain individuals produce urticaria, erythemata, and other symptoms, each of the foods producing fairly constant skin-lesions. Urticaria occurs more frequently than erythemata, fish, tomatoes, and cheese only producing urticaria, while cereals and port produce erythemata in a considerable proportion of the cases. Tomatoes and cereals usually produce the lesions within an hour after ingestion, and the eruption usually persists less than twenty-four hours.

The peculiar reactions on the ingestion of eggs, cereals, and port are inherited in a considerable percentage of the cases, and in one-half of the cases in the writer's collection of sensibility to egg ingestion the skin manifestations were accompanied by a cough and dyspnœa.

Most, but apparently not all, urticarias and erythemata following the ingestion of these proteids are due to phenomena similar to those observed in anaphylaxis.

J. M. H. M.

THE SUGAR-CONTENT OF THE BLOOD IN VARIOUS DISEASES OF THE SKIN.

H. J. Schwartz, W. J. Heimann, and H. C. Mahnken. (*Journ. Cut. Dis.*, 1916, xxxiv, p. 159.)

In this contribution the sugar content in the blood in various diseases of the skin is estimated. In recent years much interest has been manifested in the relation of the blood-sugar to various diseases, such as diabetes, nephritis, disorders of the internal secretory glands, etc.; but this is the first paper in which the sugar-content has been estimated in cutaneous diseases. It has been pointed out that a study of the sugar-content of the blood gives a more satisfactory indication of the condition of mobile sugar than does the examination of the urine, and that profound changes may occur in the sugar-content of the blood in response to conditions which do not produce glycosuria.

The blood-sugar in the normal adult varies from 0·07 to 0·11 per cent. It is definitely increased after a meal as the result of ingestion of starch and sugar.

All the ordinary dermatoses were studied from the point of view of sugar-content. Hyper-glycæmia was found to be frequent in acne, seborrhœa, and sycosis; out of 60 cases of these affections studied, 26 showed excessive blood-sugar, only 24 a normal amount, 10 being on the border-line. Only one patient with rosacea was studied in whom there was a marked hyper-glycæmia. There seemed to be a definite relation between pilo-sebaceous infections and hyper-glycæmia. In a large variety of other cutaneous affections examined, such as eczema, Erythema multiforme, syphilis, and urticaria, it was rare for the blood-sugar content to be higher than normal. J. M. H. M.

COMPLEMENT FIXATION IN ACNE VULGARIS. A. Strickler, J. A. Kolmer, and J. F. Schamberg. (*Journ. Cut. Dis.*, 1916, xxxiv, p. 166.)

The results arrived at in this research have been thus summarised by the writers:

(1) As based upon complement fixation tests with a monovalent antigen of *B. acne* (Unna-Sabouraud type), this bacillus, while apparently exciting most marked pathogenic effects in that group of lesions commonly spoken of as Acne vulgaris, is also active in rosacea, seborrhoic dermatitis, and occasionally in such diseases as vesicular eczema, Sycosis vulgaris, etc. This would seem to indicate that the bacillus is not specific for acne, but may be a normal inhabitant of sebaceous follicles capable of assuming pathogenic powers under favourable conditions in other skin diseases.

(2) With regard to the cocci recovered from the acne lesions, the reactions indicated that these cocci were not specific for acne, but belonged to the family *S. albus* and *aureus*.

(3) The complement fixation reactions also tended to show the activity of colon bacilli in certain skin diseases, particularly Acne vulgaris, rosacea, and seborrhoic dermatitis. Almost two-thirds of the cases of acne gave a positive complement fixation test with the *Bacillus coli* obtained from the fæces of acne patients. In contrast to this, only 15 per cent. of non-acneiform skin affections gave positive reactions with this bacillus, and the non-eruptive controls which were examined gave entirely negative results with this organism. With a polyvalent antigen of strains of colon bacilli recovered from the fæces of persons suffering from Acne vulgaris, the percentage of positive reactions and the degree of complement absorption were found to be higher than with the control antigens of colon bacilli from the fæces of normal persons, with the sera of persons suffering from Acne vulgaris and seborrhoic dermatitis. In Acne rosacea, as also in the eczemas, here were evidences of the activity of colon bacilli as based upon positive com-

plement fixation reactions, due apparently to the presence of antibodies in the serum, although the reactions with both antigens of colon bacilli were similar.

(4) The autogenous vaccines were prepared in accordance with the serological findings in individual cases—that is, if the serum of an individual with acne absorbed complement with the *B. acne* and *B. coli* antigens, the vaccine was prepared of these bacteria, using an autogenous vaccine of *B. coli* and a stock vaccine of *B. acne*; if complement absorption occurred with all three antigens of staphylococci, *B. coli* and *B. acne*, the vaccine was prepared accordingly.

J. M. H. M.

SPIROCHÆTES AND THEIR GRANULE PHASE. H. B. FANTHAM, M.A.Cantab., D.Sc.Lond. (*Brit. Med. Journ.*, March, 1916, p. 409.)

SPIROCHÆTES are widely distributed in Nature. Some are free-living, occurring in stagnant water or sea-water. Others live in the digestive tracts of vertebrate and invertebrate animals. Others, again, occur in the tissues of vertebrates and are often pathogenic, *e. g.* the *S. recurrentis* and *S. duttoni* are found in the blood in the pyrexial periods of relapsing fever, *S. Schaudinni* in tropical ulcers, and the *S. pallida* (*Treponema pallidum*) is found in syphilis, and the *Treponema pertenue* in yaws. Spirochætes occurring in the vertebrates may be transmitted directly by contamination (*e.g.* syphilis) or by an arthropod vector (*i.e.* relapsing and African tick fevers).

The longest spirochæte, *S. plicatilis*, a free-living species, may reach 200 μ in length, while the *S. laverani* found in the blood of mice may be only 3 μ long. Owing to processes of growth and division, the latter occurring by binary fission, there is much morphological variation among spirochætes. All spirochætes "shed granules," and this process is best investigated in *S. duttoni*, which is transmitted from man to man by the tick *Ornithodorus moubata*. Dutton and Todd outlined the process in 1907 and Leishman studied it in detail in 1909–10. Leishman showed that spirochætes give rise by multiple fission to granules or coccoid bodies inside the invertebrate host, and that these granules find their way to the Malpighian tubules, gonads and other organs of the tick. The granules multiply and the eggs of the female tick become infected and their progeny are born infected. Balfour, Fantham and Hindle have confirmed their results in *S. duttoni* and other species. Balfour observed granules in the *S. pallida* and *pertenuis*, and his observations have been confirmed by Ranken and Hoffman.

Fantham describes the process of formation of the coccoid bodies by multiple transverse fission as observed in fresh specimens of the larger spirochætes:

The cytoplasm is at first finely granular, and the chromatin bars appear as minute refractile masses. Oval concentrations of the cytoplasm occur around the chromatin rodlets, ultimately forming a series of coccoid bodies or granules, lying usually transversely or obliquely in the periplast sheath. The coccoid bodies may be set at liberty by a rupture at one end of the spirochæte or by several ruptures. The groups of coccoid bodies may retain the outline of the spirochæte from which they derive, but when released by rupture they tend to form irregular clumps. The elongation of the granules and the assumption of the sinuous form and the emergence of very small spirochætes from the groups of granules have been observed during life. Coccoid bodies may be present when spirochætes as such cannot be detected. At the same time, the finding of chromatinic granules is not sufficient to justify the inference that spirochætosis is indicated, as all such granules are not necessarily spirochætal in origin. It is essential that motile spirochætes should be found at some period of the disease, and the developmental stages leading to granules and coccoid bodies observed *in vivo*.

Marchoux and Couvy, Blanc and Wolbach consider these bodies to be degenerative changes. On the other hand, it has been shown by Sergent and Foley and by Nicolle and Blanc that the *S. recurrentis* in the body louse assumes a very small form which is as virulent as the spirochæte stage. Balfour, in 1908, found granule stages in the red blood-corpuscles of Sudanese fowls suffering from spirochætosis. Leishman, by continuous observation, has seen the extension of small and actively motile spirochætes from granule clumps in tick spirochætosis.

Noguchi (1913) demonstrated granules in pure cultures of the *Treponema pallidum*, and in 1911 showed that it was not rare to find a round body connected with one or two young pallida as though the latter were just sprouting from the former.

The value of these observations is obvious, and the further researches of the author will be awaited with interest. Full references to the papers of other writers in this branch of biology are given. J. H. S.

SYPHILIS.

SYPHILIS AND YAWS IN THE TROPICS. S. Vassallo, M.D. (*Practitioner*, April, 1916, p. 431.)

Syphilis in the tropics differs in some interesting points from that seen in Europe. A slight and latent syphilitic infection seems to be inherent in the native, latent syphilis occurs in Europeans infected by native women, and the high percentage of still-births and abortions for which no explanation is available is taken by the writer to indicate syphilitic infection. The indurated chancre and secondary rashes are seldom encountered, and tertiary manifestations in the tropics show the most various aspects. Among the organs most frequently affected are the throat and nose, the tonsils presenting all varieties of ulceration, from small superficial ulcers to deep necrosis involving and causing destruction of the organ. Deep and rapid extension in the nose must be distinguished from "Destructive ulcerous rhino-pharyngitis of the tropics" (Leys) which has been variously regarded as a sequel of yaws, or as syphilitic, leprotic, or malarial in origin. An affection occasionally seen is that of a granulomatous lesion with a raised horny fissured margin with granulations at the bottom of the fissures, enclosing irregular areas of skin showing small, more or less circular, discoloured patches. Gummata are surprisingly rare, although perhaps many ulcers begin in this way. Yaws has been considered to be syphilis modified by the tropics, but experimental investigation has proved conclusively that the two diseases are distinct, inasmuch that patients suffering from yaws may contract syphilis and syphilitics may contract yaws, and monkeys successfully inoculated with yaws do not acquire immunity against syphilis. Only slight difficulty is experienced in the diagnosis of yaws, except sometimes in the early stages when it may begin with a slight furfuraceous desquamation or a thickening of the skin. The development of the framboesoma usually follows and clears up all doubt. Yaws does not cripple the patients but at times a condition locally known as crap-pox or craw-pox occurs; this affection generally attacks the feet and causes thickening of the skin with deep fissures or small circular desquamating areas without ulceration. Both in syphilis and yaws salvarsan has proved of supreme value.

In a few cases the writer adopted a deviation from the ordinary mode of procedure by dissolving the salvarsan in 10 c.c. of sterilised water with the help of a little NaOH and injecting it directly, under local anæsthesia, into one of the dissected veins of the arm. The results obtained were identical with those obtained by the usual method. If Neisser's opinion be accepted that no matter in what form the drug is introduced its solubility in the blood is never more than $\frac{1}{1000}$ per cent., the author considers there is no reason why this method should not be adopted, as it would combine the advantages of both the intramuscular and intravenous methods of administration. S. E. D.

A FAMILY OF OCCULT SYPHILIS. W. A. Lind, M.B., B.S. (*Med. Journ. of Australia*, March 11th, 1916, p. 222.)

Mrs. X—, a married woman, aged 46 years, was received at the Hospital for Insane, Kew, Victoria, suffering from general paralysis of the insane. Her serum gave a positive Wassermann reaction. The patient's husband was certain he had never had syphilis, and his blood gave a negative reaction. There are five children. Their blood was examined, with the following results:

(1) Girl, aged 20 years—positive reaction.
(2) Boy, aged 17 years—negative reaction.
(3) Girl, aged 14 years—negative reaction.
(4) Girl, aged 10 years—positive reaction.
(5) Boy, aged 4 years—positive reaction.

When the first child was a month old Mrs. X— tried to foster-mother the child of a friend. This child tried the breast twice, but was unable to suck, and later on died of marasmus. The mother of this infant died two years later, and it has been impossible to trace the father. Very soon after the attempt to suckle her friend's child Mrs. X— developed sore breasts, and her own child developed sores on the mouth, while the vaccination took twelve months to heal There was no history that Mrs. X— had any other illness.

As regards the children—the first and fourth children show peg-top teeth, and are not strong, the second and third are normal, and the youngest child is described as having peg-top teeth of first dentition, and his skin is flabby.

J. H. S.

THE FIXATION OF SALVARSAN AND NEOSALVARSAN BY THE BLOOD AFTER INTRAVENOUS INJECTION. W. J. Young. (*Bioch. Journ.*, December, 1915, p. 479.)

The author injected goats intravenously with salvarsan or neosalvarsan, drawing off the blood at various intervals of time. Arsenic was present in the dialysed serum in every case, some arsenic being bound to the serum proteins which cannot be removed by dialysis. With reference to the time required for the arsenic to be completely eliminated from the blood the author quotes the investigations of Beveridge and Walker, who found that it could not be detected in the urine of rabbits up to the eleventh day after intravenous injection of salvarsan or neosalvarsan. Stümpke and Siegfried claimed that traces of arsenic were found in the urine of men and other animals even after several months had elapsed, but they were unable to demonstrate its presence in the blood later than twenty-four hours after intravenous injection, and they suggested that secondary deposits of arsenic were formed in the organs and then gradually excreted in the urine. Schütte stated that in horses no arsenic could be detected in the urine and fæces later than thirteen days after intravenous injection of salvarsan. Stühmer investigated the properties of serum drawn at increasing intervals after intravenous injection of salvarsan and neosalvarsan to ascertain how long after injection it was possible to detect specific therapeutic properties in the serum. He compared the different sera with regard to their protective action against trypanosome infection of mice, and at the same time tested the sera for the presence of free salvarsan by the Ehrlich-Bertheim reaction. Serum drawn as late as the seventh day after injection of salvarsan postponed the infection. With neosalvarsan after the second day the serum gave no reaction, either chemically or biologically. Thus after two days no free neosalvarsan appeared to be present in the serum. Riebes, employing Abelin's diazo reaction with resorcinol for detecting the amino group of salvarsan, found that in the majority of cases the reaction disappeared from serum three hours after the injection. The author's experiments, made to ascertain how long a time after injection "bound arsenic" could be detected in the serum, showed that this is very slowly eliminated, whereas the bulk of the neosalvarsan is quickly excreted, only a trace being present after the first twenty-four hours. His conclusions are as follows: After intravenous injection of goats with salvarsan and neosalvarsan the serum contains arsenic in a form which cannot be separated from the proteins by dialysis, and which is precipitated with the serum proteins by tannic acid. Salvarsan and neosalvarsan behave in a similar manner to atoxyl. No such combination is obtained when inorganic arsenic is injected. This combined arsenic is found in the blood long after all free salvarsan and neosalvarsan have been eliminated, it is found in the plasma and in the red blood cells, but no trace of arsenic is retained in the fibrin.

S. E. D.

THE TOXICOLOGY OF SALVARSAN. W. H. WILLCOX, M.D., B.Sc., F.R.C.P., and JOHN WEBSTER, F.I.C. (*Brit. Med. Journ.*, April 1st, 1916, p. 473).

SALVARSAN was introduced by Prof. Paul Ehrlich in 1910, and neo-salvarsan in 1912. These were also known by the respective numbers "606" and "914," denoting the numerical position of the compounds in the list of chemical substances prepared and experimented upon. On the outbreak of war it was found desirable that dioxydiamido-arseno-benzol should be manufactured in this country. The preparation of this important remedy was satisfactorily carried out and it was introduced under the name of "kharsivan." Before being placed on the market, samples of kharsivan were submitted to careful chemical and physical tests, physiological and therapeutic tests being carried out by one of the writers (W. H. Willcox) at the request of the Board of Trade, and it was found that the English preparation was practically identical with salvarsan. Kharsivan was then definitely introduced after the sanction of the Board of Trade had been received. The testing of kharsivan after its introduction was entrusted to the Medical Research Committee, who have submitted samples of every batch prepared to searching physiological and toxicological tests.

The therapeutic effect of any antisyphilitic remedy can be estimated by the application of tests for the presence of the specific organism in syphilitic lesions and by the application of the Wassermann reaction to the blood serum. These tests have shown that salvarsan or kharsivan occupy the foremost place in the treatment and cure of syphilis. It is unnecessary to emphasise the importance of these remedies from a prophylactic point of view since the rapid destruction of the infective agent in the body implies the prevention of spread of infection. Other spirochæte infections, such as relapsing fever in man, recurrent fever in animals, and spirillose infection of birds respond equally well to salvarsan or kharsivan. Yaws yields rapidly to treatment with these substances, Mycosis fungoides and glandular conditions resembling syphilis have shown marked benefit. The same may be said of tertian malaria, but quartan malaria does not seem to respond in the same way. Leukæmia, pernicious anæmia, lymphadenoma, trypanosomiasis, anthrax, psoriasis and Lichen planus have been benefited to a less degree. The authors discuss the constitution and properties of salvarsan and neo-salvarsan as well as the chemical and physiological tests, preparation, contra-indications, and the toxic symptoms apt to follow administration. With regard to excretion, salvarsan was found in the blood one hour after injection in two cases—½ mg. and ⅓ mg. of arsenic (calculated as As_2O_3) being recovered from 100 c.cm. of blood serum. Excretion takes place mainly by the kidney and bowel; arsenic is present in the urine and fæces for at least three weeks after an intravenous injection. In cases of death after salvarsan, arsenic is found in the abdominal viscera—for example, spleen, kidney, liver, suprarenal glands, etc.; it is also found in small amounts in the muscles and blood. Arsenic seems to be almost entirely absent from the brain and nervous system, so that the symptoms of profound toxæmia in cases of salvarsan poisoning are certainly not due to the action of the arsenic as such on the central nervous system. To investigate the influence of salvarsan in lactation, milk from a woman to whom two intravenous injections had been given was collected and two specimens were found to be free from arsenic. In a second case the same results were obtained. This shows that the benefit derived by a syphilitic infant from being suckled by a mother to whom salvarsan has been administered cannot be due to the presence of salvarsan in the milk and must be explained on other grounds, such as the presence of antibodies due to the destruction of spirochætes in the mother's body. Since toxicological analyses show that a full dose of salvarsan, 0·6 grm., is not completely excreted after three weeks, the authors are strongly of the opinion that an interval of four weeks should elapse between each full dose, shorter intervals giving rise to a risk of cumulative action. Before salvarsan is administered an aperient should be given, alcohol and tobacco should be avoided for twenty-four hours before and after, and the patient should remain in bed on the day the injection is given and for twenty-four hours afterwards, or until the temperature is normal. The diet should be light until all symptoms have cleared up. Serious symptoms such as collapse, twitchings, delirium or coma should be treated by an injection of normal saline intravenously or subcutaneously or by the rectum, or venesection may be performed when the blood-pressure is not low. A list of toxicological analyses and notes of fatal cases is appended. S. E. D.

THE THERAPEUTIC AND REACTION EFFECTS OF KHARSIVAN.

H. C. Lucey, M.D. (*Brit. Med. Journ.*, April 29th, 1916.)

This paper is a record of 600 injections of kharsivan given at the Royal Herbert Hospital, Woolwich. As a routine treatment for primary and secondary syphilis the writer gives three injections of 0·6 grm. at fortnightly intervals, with two weekly injections of mercurial cream. This is a short intensive course, designed to render a soldier fit for active service as quickly as is possible consistent with a reasonable chance of permanent cure. Gibbard and Harrison's statistics produced at the International Congress of Medicine, 1913, showed that on a precisely similar course, using the German preparation, only 3·9 per cent. of cases relapsed clinically and 19·4 per cent. serologically within a year of the suspension of treatment, and the writer has up to the present time had only one case return, and for a fresh infection, not a relapse. He considers kharsivan as potent as the original German preparation. The type of lesion which clears up most rapidly is one in which the blood supply is good and in which there is no breach of surface, especially infiltrations around the mouth and nose. Primary sores are rendered inactive after one injection, those on the skin taking rather longer to heal than those on mucous membranes, the average time when some local application is used being fifteen days. The activity of a rash is immediately checked after the first injection and disappears in a few days or weeks, condylomata and mucous patches usually clearing up within a week. Enlarged lymphatic glands are reduced at the end of a course of treatment, but incomplete reduction does not imply incomplete destruction of the *Treponema pallidum*, as shown by the absence of relapses in the great majority of such cases.

Patients are injected in groups, the same technique and dosage being employed, so that each case serves to control the others. Freshly distilled water was used throughout, and except in a few cases the full dose (0·6 grm.) dissolved in 200 c.cm. of saline has been given. In no case has one full dose followed another at a shorter interval than fourteen days. No breakfast is allowed previously to the injections and bed for twenty-four hours and no food for six hours has been the rule. The absence of unpleasant symptoms in the great majority of cases was very striking, 72 per cent. being followed by no symptoms whatever. As regards pyrexia the freshness of the infection as well as the degree of infection are factors determining a reaction. Headache occurred in 17 per cent., rigor in 5 per cent., vomiting in 7 per cent., diarrhœa in 10 per cent., and transient albuminuria developed in ·3 per cent. Herxheimer's reaction occurred in 2·3 per cent. Herpes labialis was noted in one case, and one developed a mild dermatitis. Thrombosis of the vein at the site of injection occurred in 0·5 per cent., and a reaction probably due to an abnormal arsenical toxicity in a particular batch of kharsivan occurred in ·5 per cent. S. E. D.

THE TREATMENT OF VENEREAL DISEASES IN THE ARMY.

Major E. G. Ffrench, R.A.M.C., M.D., F.R.C.S. (*Practitioner*, May, 1916, p. 452.)

On the admission of patients to the Military Hospital, Rochester Row, a routine practice is made of examining chancres for the *Spirochæta pallida* both by dark ground illumination and by the Indian ink method. It is not always possible to demonstrate spirochætes at the first examination because they are not always present in the chancre. In some cases an examination every day for five or six days is required before they come sufficiently near the surface of the chancre to be squeezed out in the serum. It is unwise to conclude that a chancre is syphilitic because it is indurated; on the other hand, a large number of soft looking chancres are diagnosed as syphilitic by this method. As soon as the diagnosis is made the patient is prepared for an injection of salvarsan or kharsivan and ·4 grm. is administered. On the following day, 1 gr. of metallic mercury in cream, m. 5, is injected into the gluteal region. The patients get four weekly doses of salvarsan of ·4 grm. or five weekly doses of ·3 grm. followed by an injection of mercurial cream the next day. The mercurial injections are kept up for another five weeks, making a total of nine injections. Kharsivan, novarseno-benzol (Billon) and galyl are now being used in doses equivalent to ·4 salvarsan with equally satisfactory results. Neo-salvarsan, arseno-benzol and galyl are given in concentrated solution with 10 c.c. of freshly distilled water. Hectine has also been used with marked success in some cases of intractable syphilis. Intramine has been given in a few cases, but sufficient time has not elapsed to enable a definite opinion to be formed on the value of this preparation.

The author gives tables showing the results of the Wassermann tests two and four months after completion of a course of treatment. The primary cases, almost without exception, gave a negative reaction after two months and remained so when the second test was performed at the end of another two months. The secondary cases show a higher percentage of negative results after the first and second tests, but many of the tertiary cases were positive after the first and second test, showing that it is seldom that a positive reaction, in a case of tertiary syphilis, is converted into a negative after a course of treatment or even after several courses. The earlier the stage of the disease in which treatment is started the higher is the percentage of negative reactions obtained. Sixty cases of venereal lesions, syphilitic and non-syphilitic, were treated by the Simpson lamp, and this method is regarded by the writer as a great help in shortening the duration of treatment. Intraspinal injections of mercurialised serum containing $\frac{1}{50}$ gr. hydrarg. perchlor. in 30 c.c. sterilised horse serum have been administered to a series of cases of cerebral and spinal syphilis with good results. The remainder of the paper is devoted to a description of the methods employed in the treatment of gonorrhœa and gonorrhœal rheumatism, and the electrolytic method is receiving a thorough trial. S. E. D.

THE TREATMENT OF SYPHILIS IN THE ARMY; WITH SPECIAL REFERENCE TO THE ADMINISTRATION OF "606" IN CONCENTRATED SOLUTIONS. Captain H. McGrigor, R.A.M.C., M.D., D.P.H. (*Practitioner*, May, 1916, p. 462.)

This paper is a report of the work done at the Connaught Hospital, Aldershot, from September 6th, 1914, to December 31st, 1915. Of cases of syphilis there were 1084 new admissions and 89 transfers. All cases of syphilis were treated in hospital until they were free from active manifestations, the average time to accomplish this being 15·5 days. On leaving, all patients had to attend every week for mercurial and other injections. In practically all the new cases of syphilis a definite Hunterian chancre was present, and great clinical importance was attached to the hard india-rubber induration on grasping the lesion between the forefinger and thumb. No other ordinary ulcer or genital sore uncomplicated with syphilis gave this india-rubber feeling on palpation.

The presence of headaches was inquired into very carefully; 14·7 per cent. of all cases had definite headache, mostly nocturnal and of an ill-defined character; no cases presented iritis or other eye complications. In most of the old cases, even when the disease had been contracted from eight to twenty years before, enlargement and shottiness of the glands could be demonstrated, and a valuable point in diagnosis of any condition which could be regarded as secondary syphilis was that no one clinical condition, such as skin infiltration or affection of mucous membranes or bones, was ever found without accompanying enlargement of the glands of the neck, groin and elbow.

One complete course of treatment was given to all cases, and after one such course a case was considered fit for active service, no active signs being present and no likelihood of further treatment being required for several months or a year.

The first injection of mercury was always given just before the "606" injection, and no special preparation of the patient prior to the latter was considered necessary. A small amount of albumin in the urine was not considered a contra-indication to the injection of "606" or kharsivan. A number of patients whose urine did not clear up satisfactorily under mercury were given the full dose of salvarsan even though the urine was loaded with albumin, and subsequent improvement indicated that the albumin was of syphilitic origin. For neo-salvarsan 10 c.c. of ordinary tap-water at 60° F. was used; tap-water was also employed for salvarsan or kharsivan, the lime salts being allowed to deposit after boiling, the clear water syphoned off, made into saline and again boiled and filtered through sterile gauze to remove further lime salts. In the tropics the writer has used clean rain-water, and no untoward results have followed from the use of either this or boiled tap-water. To distend the veins, when this is necessary, the patient is directed to swing the arm round the head, or to hold the arm under the hot-water tap, or to open and close the fist. When these measures fail, the tourniquet is put on high up near the shoulder and a few turns of an Esmarch bandage are applied from the shoulder downwards and the fingers upwards. The needle is introduced under the skin first and then pushed into the vein. When the quantity of solution is from 50 c.c. to 250 c.c. it is run in by gravity, when less than 50 c.c. injected by means of a "Record" syringe. The total number of injections of salvarsan, neo-salvarsan, kharsivan and neo-kharsivan given during the period was 2095. For a time one "606" then 9 Hg. followed by one "606" were given, but later, one "606," two Hg., one "606," two Hg., one "606" and one Hg. The latter method is completed in one month, the former taking nine weeks. The reactions noted were rigor, headache, vomiting, diarrhœa, and a rise of temperature of 100° F. or over on the day of injection and following day. The author states the results in percentages according to the nature of the preparation and the quantity and quality of the medium employed. In contrasting the results from the injection of kharsivan in 250 c.c. distilled water saline with those from the same preparation in 250 c.c. boiled tap-water saline, the result was in favour of the latter. When kharsivan was dissolved in

100 c.c. distilled water saline as against the same quantity of boiled tap-water saline, the result also showed in favour of the latter. Kharsivan dissolved in 20, 50, 100 and 250 c.c. distilled water saline was in favour of 20 c.c. etc. After a large series of experiments the author is of the opinion that the total knowledge gained is not very great but serves to emphasise the fact that the reactions are not really much affected by the quantity or quality of the medium used, and the experience has been gained that boiled tap-water can be used with safety and the quantity of the medium can be reduced with safety and even profit.

S. E. D.

INTRAMINE: A NEW ANTISYPHILITIC REMEDY. HAROLD SPENCE, M.D. (*Lancet*, April 22nd, 1916.)

THE writer gives an account of the origin, chemistry, properties, and administration of "intramine" or di-ortho-amino-thio-benzene with the results he has obtained from the use of this remedy in a series of sixty-five cases of syphilis. Intramine is administered intramuscularly, suspended in oil in the proportion of 1 grm. in 10 c.c. Doses up to 12 grm. have been given, but the full therapeutic effect is obtained with 1 or 2 grm., repeated in a few days if required. Local pain after injection is a variable symptom, some patients complaining of severe and persistent pain, others of only a slight stiffness. From twenty-four to forty-eight hours after administration a rise of temperature and some malaise may be looked for, but the thermometer reading rarely exceeds 103° F. The induration at the site of injection disappears in a few days, and with ordinary aseptic care there should be no sloughing; in the writer's cases there has been none. The field for the remedy is especially the later stages of syphilis where metallic compounds alone are less useful, 1 grm. of intramine being followed on the third or fourth day by a metallic preparation given intravenously. In the author's experience, however, the lesion has not infrequently healed before the arsenical or other preparation could be given. Most of the cases summarised are of this type. In primary syphilis the writer has found intramine of little effect. Given after a metallic preparation it may occasionally accelerate the disappearance of a secondary papular rash and the induration of a large sore of the Hunterian type. It seems also to influence favourably superadded ulcerative conditions.

The author concludes that intramine is an efficient symptomatic remedy, particularly in later secondary syphilis and its complications, and in recurrent and tertiary lesions. It appears also of value in cerebro-spinal syphilis. It has proved effective in some chronic processes non-syphilitic in character, *e. g.* Lupus vulgaris and chronic leg ulcers. S. E. D.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

ERYTHEMAS, INFLAMMATIONS, ETC.

Atonic Wounds and their Treatment. F. DEBAT. (*Paris Médical*, 1916, vol. xix, p. 450.)

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Hard Œdema (edemo duro). E. Serra. (*Gazz. d. Ospedali e d. Clin.*, Milan, December 23rd, 1915, vol. xxxvi, p. 1441.)

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Salvarsan Application, A Simple Method of. J. Schumacher. (*Derm. Wochenschr.*, October 23rd, 1916, lxi, p. 997.)

Syphilis in African Native Tribes and among Native Workers on the Rand, Treatment of. H. Bayon. (*Trans. of Soc. of Tropical Med. and Hygiene*, April, 1916, ix, No. 6, p. 187.)

Syphilis in the Army, with Special Reference to the Administration of "606" in Concentrated Solutions; Experience in the Treatment of. H. J. McGrigor. (*Trans. of Soc. of Tropical Med. and Hygiene*, April, 1916, ix, No. 6, p. 161.)

Syphilitic Alopecia, with Report of Case. Complete. Loyd Thompson. (*Journ. Amer. Med. Assoc.*, April 22nd, 1916, lxvi, p. 1303.)

Test for Syphilis and its Comparison with the Wassermann Reaction, A Urinary. Carl D. Gray. (*Med. Record*, May 6th, 1916, p. 821.)

Toxicology of Salvarsan: Dioxydiamido-arseno-benzol (Salvarsan or Kharsavan). W. H. Willcox and J. Webster. (*Brit. Med. Journ.*, April 1st, 1916, p. 473.)

Tuberculin Treatment of Early Syphilis. M. Brach. (*Wien. Klin. Wochenschr.*, December 9th, 1915, xxviii, No. 49.)

Syphilis and Yaws in the Tropics. S. Vassallo. (*Practitioner*, April, 1916, p. 431.)

REVIEWS.

THE MEDICAL ANNUAL.*

THE volume for 1916 has made its appearance with its usual punctuality, and continues to supply valuable information in all fields of medicine. Needless to say, naval and military subjects are much to the fore, but this does not prevent full attention being given to non-military matters.

The articles on dermatological subjects are from the pen of Dr. Graham Little, as in former years, and their high standard is in no way diminished. We note, however, that most of the articles deal with reports from English and American sources, and we presume that this is due to the difficulty in obtaining Continental journals. Mr. C. F. Marshall is still responsible for articles on syphilis, and we are rather surprised that so little is said with reference to the substitutes for salvarsan, a subject which is of considerable interest to the general practitioner. We are sure that this volume will not fail to appeal to a large circle of medical men.

THE PATHOLOGY OF TUMOURS.†

THIS is an excellent little book. It gives a general outline of the pathology of new growths in a way which will appeal to every student. The matter is well arranged in three parts: (1) The General Biology of Tumours, (2) The General Pathology of Tumours, and (3) The Special Pathology of Tumours. Each part is dealt with from an elementary standpoint and no effort is made to make out a case for any particular theory. The descriptive work is good, and the illustrations are well chosen and excellently reproduced. We can confidently recommend it to all students and practitioners who wish to obtain a comprehensive survey of this important subject.

THE MORTALITY FROM CANCER THROUGHOUT THE WORLD.‡

WE have received a copy of this work which, we learn from the Preface, was published by the Prudential Assurance Company of America as their contribution to the educational efforts of American Society for the Control of Cancer. The work has been prepared by Mr. F. L. Hoffman, the Statistician to the Company, and is undoubtedly the latest and probably the most complete work on the subject. The objects of the book, we are informed, are to make existing statistical data available to the student of the subject, to whom most of the facts would otherwise be inaccessible; to determine the true tendency of the cancer death-rate; and to ascertain as far as possible the relative incidence of cancer according to organs or parts of the body affected, with due regard to age and sex,

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[*] *The Medical Annual.* Bristol: John Wright & Sons, 1916. Pp. cxii + 920. Price 10*s.* net.

[†] *The Pathology of Tumours.* By E. H. KETTLE, M.D. London: H. K. Lewis & Co. Ltd. Pp. viii + 224. 126 Illustrations. Price 10*s.* 6*d.* net.

[‡] *The Mortality from Cancer Throughout the World.* By F. L. HOFFMAN, LL.D., etc. Newark, New Jersey: The Prudential Press. Pp. 826.

in different countries of the world. The reader himself must judge how far the objects have been attained, and he will find a mine of information at hand. To the dermatologist the chapter on "Cancer and Occupation" will appeal, as will also the final chapter entitled "Observations and Conclusions."

We understand that this extremely valuable book has not been put on the market, but is presented gratuitously by the Prudential Company to libraries and certain individuals interested in cancer problems. We may take this opportunity of congratulating the Company and its Statistician on the production of this extremely interesting work.

BOOKS RECEIVED.

Estude clinico do Granuloma Venéreo (These inaugural). By Dr. H. C. De Souza Araujo. Brazil: Instituto Oswaldo Cruz. Caixa Postal 926. Price not stated.

Links in a Chain of Research on Syphilis. By J. E. R. McDonagh, F.R.C.S. London: Harrison & Sons. Price 5*s.* net.

The Pathology of Tumours. By E. H. Kettle, M.D., B.S. With 126 Illustrations (3 in colours) from original drawings and photographs. London: H. K. Lewis & Co. Ltd., 136, Gower Street, W.C. Price 10*s.* 6*d.* net.

The Medical Annual, 1916. Bristol: John Wright & Sons, Ltd. Price 10*s.* net.

The Mortality from Cancer throughout the World. The Prudential Insurance Company of America. Home Office, Newark, New Jersey.

NEW PREPARATION.

Bynogen.

Messrs. Allen & Hanbury have sent us a sample of this preparation, which is said to be a combination of 75 per cent. milk protein, 20 per cent dextrin-maltose, 2 per cent. each of glycerophosphates of soda and lime, and 1 per cent. glycerophosphate of magnesia. The preparation is a white crystalline powder and is very palatable. It should prove a useful food in debilitated conditions.

THE BRITISH
JOURNAL OF DERMATOLOGY.
JULY–SEPTEMBER, 1916.

THE RATIONALE AND PRACTICE OF CHEMOTHERAPY.*

By J. E. R. McDONAGH, F.R.C.S.

Introduction.

My reason for introducing the subject of chemotherapy is one prompted by circumstances. The war has prevented us from relying upon Germany, and in consequence of this we have had to shift for ourselves. Some have been content to imitate German empiricism with incomplete success, while others have attempted to place the subject upon a logical basis. Although the result of these logical endeavours may not at present be all that is desired, time will no doubt improve them. Anyhow, invention is the only thing which will redound to the credit of British medicine: imitation, however successful, will never do so.

The prevailing view of chemotherapy is shortly this: arsenic is essential, and cures syphilis—a disease, by the way, for which it was not originally thought suitable, owing to its parasitotropic and to its non-organotropic properties. I will therefore ask those who have kindly come to take part in the discussion to answer the following questions:

(1) Why was arsenic the element chosen, otherwise than for the reason that it was at the time the only drug known which was of any value in the treatment of sleeping-sickness, the disease for dealing with which chemotheraphy was inaugurated?

(2) Why were several hundred compounds tried before a suitable one was found, otherwise than for the reason that Ehrlich had no sound basis upon which to work?

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* Being a paper read at the Royal Society of Medicine on April 13th, 1916.

(3) Why does salvarsan not cure syphilis when its spirillocidal action is so strong?

(4) Why should arsenic exhibit a chemical affinity for parasitic cells—and, it is to be remarked, for only certain parasitic cells—and not for the cells of the host? In other words, why is salvarsan parasitotropic and not organotropic, and why only parasitotropic for certain parasites?

My answers to the first two questions are contained herein. My answer to the third question is that syphilis is not cured by salvarsan because the *Spirochæta pallida* is not the cause of the disease. My answer to the fourth question is that salvarsan is more organotropic than parasitotropic, and that it is only parasitotropic for certain parasites owing to the chemical constitution of those parasites.

Although chemotherapy is to be the main theme of my paper, I should like to say that it is only one of the links in my chain of research upon syphilis. The first link of that chain was the discovery of the *Leucocytozoon syphilidis* in 1912. The next link was formed by a chemical study of this organism, about which a few words must be said, as the points revealed in this study laid the foundation upon which the rest of my work was built. I found that the phases of the *Leucocytozoon syphilidis* consisted mainly of lipoid-globulin molecules, which proved themselves to be more resistant to reagents than the lipoid-globulin molecules of the host's cells—viz. the protoplasm of the plasma cells and of the nucleoli. Further, that their reducing action was also greater, especially in the case of the spirochætal phase, owing to its containing in its molecules a fatty acid not completely saturated.

The parasitic lipoid-globulin molecules were found to be combated by certain lipoid-globulin molecules of the host, which are formed by the lymphocytes. Some of the host's lipoid-globulin molecules are destined, in the form of plasma cells, to attack those of the parasites locally, while others circulate in the serum, in which they form the internal phase, as the resisting substance or the antibody.

The action of the lipoid-globulin molecules which circulate in the serum is general, but in other respects it is the same as that exhibited by the plasma cells. The host's lipoid-globulin molecules have a stereo-chemical molecular configuration, homologous to those of the parasite. This fact explains specificity.

The lipoid-globulin molecules which circulate in the serum are colloidal particles, which are kept in "solution" by the water their molecules contain and by the ions which are attached to them. In this form they are known as emulsoids. The fluid medium in which the emulsoid particles circulate is known as the external phase, and consists mainly of water or, let us say, of hydrogen and hydroxyl ions, which constitute the substance we call water ($H_2O = H^{\cdot} + OH'$). In order to keep the particles of the internal phase in "solution" it is necessary for the external phase to maintain a balance between the hydrogen and hydroxyl ion concentration. This balance is known as the normal hydrogen ion concentration. There are normally more hydroxyl ions than hydrogen ions in the external phase, hence the reason why serum is always on the alkaline side of neutrality.

This normal hydrogen ion concentration is maintained, on the one hand, by the free ions of the external phase, and by the adsorbed ions of the internal phase. The former constitute the so-called end-piece of complement and the latter the so-called middle-piece of complement, which is better designated as the oxidase-reducase system.

The parasites are killed by the lipoid-globulin molecules of the host by a chemico-physical process which is known as adsorption.

Adsorption is regulated by three factors:

(1) The stereo-chemical molecular configuration of the adsorbed molecules. For the adsorption to be perfect, the molecules must have an homologous stereo-chemical molecular configuration, and this is mainly regulated by the amino groups (NH_2).

(2) The permeability of the adsorbed molecules. The more permeable the molecules the easier the adsorption. Permeability is mainly regulated by the carboxyl groups (COOH).

(3) The amount of active oxygen. Adsorption is an action in which energy is used, and similar to all such actions it requires active oxygen. Active oxygen is formed directly by ferments which are known as peroxidases. Peroxidases are hydroxides of metals, and they form active oxygen provided a peroxide is present. The peroxide is formed directly by ferments, which are known as perhydridases. Perhydridases are non-metals, and they form peroxide by their action upon hydrogen and hydroxyl ions.

A peroxidase is an oxidising agent and a perhydridase is a reducing agent—hence the meaning of the term oxidase-reducase system.

The phenomena which follow the adsorption between the parasitic lipoid-globulin molecules on the one hand, and the lipoid-globulin molecules of the host on the other hand, *in corpore* are not the same as those which occur in a test-tube when an antigen meets its antibody. In a test-tube, either the antigen or the antibody is less emulsoid than when in the body; consequently when to such particles perfect emulsoid particles are added, in the shape of complement, the perfect emulsoid particles attempt to bring the imperfect emulsoid particles into their perfect emulsoid state. As this action deprives the lipoid-globulin molecules, which constitute the complement, of some of their ions, which they are not able to replace as they are when *in vivo*, all the colloidal particles concerned change their colloidal state. The previously emulsoid particles now become suspensoid particles. Suspensoids are not kept in "solution" like emulsoids, so the particles become precipitated. Such a change causes considerable alteration in the surface tension, a change which can be readily seen if red blood corpuscles form either the antigen or the antibody. Hæmolysis is the change observed.

It is now evident why agglutination, precipitation, complement-fixation, etc., are the pictures given by the immunity reactions *in vitro*.

If the tests just mentioned are specific, it is necessary for the molecules of the antigen to possess a stereo-chemical molecular configuration homologous to those of the antibody.

Since the antigen in the Wassermann reaction does not possess particles having a stereo-chemical molecular configuration, homologous to those of the reagin, how is it that fixation of complement occurs when such particles meet?

The antigen particles in the Wassermann reaction are adsorbed by the syphilitic lipoid-globulin molecules solely in virtue of the increased size, number, and adsorptive capacity of such molecules. Complement is destroyed in the attempt made by the syphilitic emulsoid particles to bring the adsorbed antigen particles into "solution." If the host's lipoid-globulin molecules are not sufficiently powerful to kill all the parasites early in the disease, when their oxidising action is greatest, they will naturally attempt to increase their adsorptive capacity and their supply of active oxygen. The particles can only do this by increasing their permeability and reducing action, and this they do by increasing their carboxyl groups. This is the reason why the Wassermann reaction is more positive in late than in early cases of syphilis. There are so many other factors which I have not time to mention here influencing the Wassermann reaction that it is certain that a positive reaction is no certain indication of active syphilis or that the patient requires treatment. The Wassermann reaction does not give us an indication of the colloidal state of the lipoid-globulin molecules or a measure of their number, the knowledge of which is necessary both for diagnostic purposes and for regulating treatment. This difficulty has fortunately been overcome by the discovery of the emulsoid-gelation reaction—or the "gel" test, as I have called it for short. The outstanding feature of my research work, as I have described it up to this point, is that the lipoid-globulin molecules of protozoal diseases, especially syphilis, are larger, more numerous, and have a greater adsorptive capacity than normal lipoid globulin molecules, or the lipoid-globulin molecules of bacterial diseases.

Natural and Artificial Protection.

When a man runs the risk of becoming infected with syphilis, there must always be, first of all, a struggle between the cells of that man and the spores of the leucocytozoon. If the former win, then, of course, there is no infection. Assuming that the latter win, the spores, having gained a firm foothold, will develop at their host's expense and produce a lesion which we call a chancre. A further development of these spores will lead to a generalisation of them in the body of the host, with a result that lesions will occur all over the body. Instead of the development going further still, the tide turns in favour of the host, and the number of the parasites gradually becomes lessened, with the result that the lesions disappear. The turning of the tide is due to the fact that the host's lymphocytes have been able to manufacture lipoid-globulin particles, the stereo-chemical molecular configuration of which is homologous to that of the lipoid-globulin molecules of the parasite.

Two questions now arise: (1) What is the nature of the primary struggle? (2) What is the *modus operandi* of the turning of the tide?

There are only two factors which come into play in the adsorption between the antigen and the antibody *in vivo*: (1) hydrogen ion concentration (oxidase-reducase system); (2) specific amino groups.

In the primary struggle the second factor cannot possibly play a part, since it takes some time for the amino groups in the lipoid-globulin molecules to be arranged in a specific manner. Moreover, the primary struggle is a local affair, a struggle between spore and cell, while the turning of the tide is a general affair—a struggle between the lipoid-globulin particles of the serum generally, of the plasma cells locally, and those of the parasites.

When a syphilitic spore enters the human body it must, in order to develop, enter a connective tissue cell or an endothelial cell. To enter a cell it must alter the surface tension of that part of the cell where it is going to enter, and this will mean a local disturbance of the normal hydrogen ion concentration. It is certain that most cells require and use oxygen, and that most cells in exchange for oxygen exhale carbon dioxide. Should a spore be able to take some of the oxygen required by the cell it tries to enter, the normal ratio between the oxygen and the carbon dioxide of that cell will cease to exist, with the result that the normal hydrogen ion concentration, or the oxidase-reducase system, will be locally and temporarily deranged, so that the spore wins, and the local surface tension of the cell will be such that the spore is easily able to enter it.

How this temporary derangement of the oxidase-reducase system can be directly prevented is not at present clear, but from the analogy with experiments I have undertaken in another direction (anaphylaxis), the derangement can be indirectly prevented by increasing the stability of the permeability, and this can be done by intravenous injections of calcium chloride.

In this connection it is interesting to note how the risk of contracting a venereal disease increases if the patient is under the influence of alcohol, owing to the fact that alcohol has exactly the opposite effect to the salt just mentioned. It is highly probable, but not so practicable, that if a patient had an injection of calcium chloride, or if he took large quantities of sodium chloride, before having connection, that his chances of contracting a venereal disease would be considerably diminished.

The *modus operandi* of the turning of the tide is probably as follows: Both the lipoid-globulin particles of the syphilitic phases and of the serum have an oxidase-reducase system. In the case of the former, the active oxygen is used by the nucleus for propagation purposes. In the case of the latter, there being no nucleus, the active oxygen is used for that purpose for which the particles exist—namely, for the purpose of adsorption. Since the amino groups have the same arrangement in the two kinds of lipoid-globulin particles, the necessaries for the physical action of adsorption will be at their best. As the active oxygen in the host's lipoid-globulin molecules will be only required for this physical action, it will follow that the host's lipoid-globulin molecules will have an advantage over those of the parasite, with the result that the changes which the spore caused the cell it was attacking to undergo in the primary struggle will now affect the parasites themselves.

If these views are correct, we should be able to forestall the turning of the tide and to hasten it, by increasing the amount of active oxygen in the lipoid-globulin particles in the serum of the host. This can be done—(1) directly, by the administration of strongly adsorbed metallic compounds, which act as peroxidases and produce active oxygen; (2) indirectly, by the administration of a strongly adsorbed non-metallic compound, which acts as a disulphide and produces peroxide and active hydrogen.

This now brings me to discuss the rationale of chemotherapy in syphilis.

RATIONALE OF CHEMOTHERAPY.

It will be remembered that, in the "side-chain" theory, Ehrlich considered the union between the antibody and the antigen was due to chemical affinities which each of these bodies possesses for each other. Then Ehrlich conceived the idea that this principle could be applied to treatment, and the application of this later received the name of "chemotherapy." This principle was shortly this: To find drugs, the chemical groups of which would combine with the chemical groups of the parasites to be attacked, without combining with the chemical groups of the host's cells. The chemical groups both of the drugs and of the cells received the name of "chemoceptors." The disease which Ehrlich hoped to combat was sleeping-sickness, and since arsenic was the body which appeared to have the greatest influence upon the disease, experiments with this metal were undertaken.

For some time after the commencement of his experiments, Ehrlich appears to have been of opinion that the sole receptors between the chemical groups in the protoplasm of the parasites and in the drugs used were the arsenic receptors. How Ehrlich could ever think that arsenic would find its chemical affinity in the protoplasm of cells and, it is to be remarked, of only certain cells, is difficult to understand; and it is surprising that most of us should still consider that this element is of paramount importance in the synthetic antisyphilitic remedies. That other receptors existed as well was shown only when it was noted that the action of arseno-phenyl-glycine was not affected by previously subjecting the parasites to the action of the arsenic derivative of phenyl-oxy-acetic acid. Then it was assumed that acetic acid receptors also existed. Since fatty acid receptors were said to exist in the protoplasm of the parasites, it was only logical to suppose that amino-acid receptors would also be found there. Working upon this hypothesis, Ehrlich discovered salvarsan.

According to Ehrlich, salvarsan works by means of its arsenic receptors and its ortho-amino-phenol receptors. When it was discovered later that a certain drug had a fatal action on one kind of parasite and not upon another kind, although in both instances a "combination" occurred between the drug and the bodies of the parasites, some further explanation of the action of salvarsan was required. Consequently, salvarsan was stated to act in the following way: The arsensic was considered to be the toxophore group, the benzene-ring to be the carrier, and the amino groups the haptophore groups.

Summing up Ehrlich's views as to the mode of action of salvarsan, we find that a union takes place between the drug and certain parasites, with a destructive action upon the parasites. What the nature of the union is, and why the death of only certain parasites should follow, are not explained.

Before discussing the mode of action of the antisyphilitic drugs, I will briefly recapitulate what I have already said concerning the way in which the body naturally protects itself against syphilis. The protective power of the body can be divided into two groups: (1) The power which acts generally—*i. e.* the lipoid-globulin molecules of the serum; (2) the power which acts locally—*i. e.* the plasma cells. The plasma cell is typical of chronic inflammation, whatever be the cause. In all instances the plasma cell is the same morphologically, but, although its gross action is similar in every instance, it is nevertheless specific in each case. To be more exact, one should call the specificity a group specificity, not an individual specificity, since the plasma cells behave in trypanosomiasis in the same manner as in syphilis, and also in some other diseases. This specificity exhibited by the plasma cells is the same as that exhibited by the lipoid-globulin molecules of the serum, and, so far as it concerns chemotherapy, it is solely due to certain physical properties which these two protective powers possess in protozoal diseases.

The lipoid-globulin molecules in the serum of protozoal diseases, especially in syphilis, are characterised by their large size and their increased adsorptive capacity. As the disease becomes more and more chronic, the size of the molecules and their adsorptive capacity increase. As has already been explained, a parasite is vanquished *in vivo* by a change which takes place on its surface. This change causes a local alteration of the surface tension, which so disturbs the normal permeability that the organism perishes. This change is brought about by adsorption. Like most physical and chemico-physical reactions, the phenomenon of adsorption is dependent upon active oxygen. Therefore some ratio exists between the destructive power of a molecule and its supply of active oxygen. In the early stages of the disease it is naturally to be expected that the supply of active oxygen will be as great as the body can manage without extra assistance. If the supply of active oxygen is not sufficient to rid the host of its parasites, the disease becomes chronic, and, all the direct methods of producing active oxygen having failed, the host is obliged to obtain it indirectly. Active oxygen is obtained indirectly by increasing the reducing action; hence the reason why the lipoid-globulin molecules are larger, and have a greater adsorptive and reducing action in late than in early cases of syphilis.

There are three actions exhibited by the lipoid-globulin molecules in the serum: (1) Adsorption; (2) oxidation; (3) reduction. In virtue of the size and of the increased adsorptive capacity of the anti-protozoal lipoid-globulin molecules, it will follow that their powers of oxidation and reduction may be enhanced by oxidising and reducing agents, and that a ratio must exist between the amount of active oxygen and active hydrogen produced and the degree of the adsorbed state in which are the oxidising and reducing agents.

The active oxygen formed by the lipoid-globulin molecules can be seen in the two following equations:

$$\mathrm{R.Fe} + 4\mathrm{H_2O} = \mathrm{R.Fe(OH)_3} + 4\mathrm{H}^{\cdot} + \mathrm{OH}'$$
$$\mathrm{R.Fe(OH)_3} + 5\mathrm{H} + 2\mathrm{H_2O_2} = \mathrm{R.Fe} + 6\mathrm{H_2O} + \mathrm{O}''$$

The active hydrogen formed by the lipoid-globulin molecules can be seen in the two following equations:

$$2\mathrm{R.SH} + \mathrm{S} = \mathrm{H_2S} + \mathrm{R.S.S.R.}$$
$$\mathrm{R.S.S.R.} + 2\mathrm{H} + 4\mathrm{OH} = \mathrm{R.S.} + \mathrm{R.SH} + 2\mathrm{H_2O_2} + \mathrm{H.}$$

From the above equations, which are only intended to be diagrammatic, it will be noted that non-metals increase the production of active hydrogen. Therefore, from what has gone before, it will now be seen that extra active oxygen can be produced in the serum of the host, directly by the administration of strongly adsorbed metallic compounds, and indirectly by the administration of strongly adsorbed non-metallic compounds. Without treatment, the lesions of syphilis vanish, because the lipoid-globulin molecules of the serum and the plasma cells contain a stereo-chemical molecular configuration homologous to those of the parasitic lipoid-globulin molecules, an homology which is necessary for perfect adsorption, and because they contain active oxygen necessary for the adsorption, which is formed directly by an iron hydroxide and indirectly by a disulphide.

Since we do not know the chemical formula of protozoal lipoid-globulin particles, it is impossible to synthesise a compound homologous with them. Therefore the only way in which we can assist the host is to increase his supply of active oxygen, and this we do directly with arsenic, aluminium, and iron, possibly also with antimony and mercury, and indirectly with iodine and sulphur.

Treatment, then, assists the host's resistance by increasing his amount of active oxygen. Therefore, treatment destroys the parasites indirectly, and not directly, as Ehrlich thought. The only phases killed directly, and these only by the metallic compounds, are the adult male phase and the female phase after impregnation. These phases are killed directly owing to the free hydroxyl groups their molecules contain. The free hydroxyl groups occur because some of the fatty acid groups are unsaturated owing to the important function these two phases have to perform. It is owing to the presence of these free hydroxyl groups that the *Spirochæta pallida* and the female cell after impregnation and not the other phases stain with silver nitrate in Levaditi's method of staining. The silver being a positive ion readily fixes on to the negative hydroxyl ion, and as the arsenic in salvarsan, the aluminium in aluvine, and the iron in ferrivine, are trivalent positive ions, it can be understood how readily they will adsorb free negatively charged hydroxyl ions.

The question might now very naturally be asked: If the action of salvarsan is in indirect one, why should arsenic be more active than mercury, since under ordinary circumstances the latter is a more powerful antisyphilitic remedy?

In my opinion, arsenic acts as a catalyst—*i. e.* it accelerates a reaction going on spontaneously, but more slowly without its assistance. Mercury possibly acts in the same way, but in virtue of its high atomic weight its action is more probably felt in the influence it exerts on mechanical adsorption. X-rays and radium probably act in malignant disease as mercury does in syphilis.

A ratio exists between the intensity of action of a catalyst and the degree of the colloid state of the catalyst. In salvarsan the arsenic is in a colloidal state; hence its action would necessarily be greater than that of any mercurial compound which we are in the habit of using. The proof of what has been said can be found if we compare the action that different manganese compounds exert on plant oxidases. Manganese formate, for instance, has nothing like such a powerful accelerating action upon plant oxidases as has manganese hydroxide. The latter is colloidal, but the former is not.

In many other synthetic organic arsenical compounds, the arsenic is also in a colloidal state, but the action of the drug is very inferior to that of salvarsan. This fact therefore at once suggests that salvarsan, when injected, becomes fixed to the substance which the arsenic is going to accelerate, and proves that a ratio exists between the therapeutic action of a drug and the degree of its adsorbed state.

Since the "606" molecule enters into adsorption with the lipoid-globulin molecules of a syphilitic serum and of the plasma cells in a case of syphilis, it will be seen that Ehrlich's statement that the drug is parasitotropic only and not organotropic cannot hold good. For a drug to be parasitotropic it must be organotropic; indeed, its organotropic properties are far more important than its parasitotropic properties.

Salvarsan and the other antisyphilitic remedies are not specific in the sense that a vaccine is specific, and the attachment of these compounds to the syphilis parasites, to the plasma cells, and to the lipoid-globulin molecules in a case of syphilis is not due to an homologous stereo-chemical molecular configuration between the adsorbed molecules, since for one thing alone the synthetic compounds are optically inactive bodies.

In the case of syphilis and in all protozoal diseases, the lipoid-globulin molecules are bigger and have a greater adsorptive capacity than the lipoid-globulin molecules in the serum of bacterial diseases. I do not wish to infer that there is a hard and fast line between protozoal and bacterial diseases, since in chronic bacterial diseases the lipoid-globulin molecules of the serum approach in their action those in protozoal diseases, since the continued use of oxidising and especially of reducing agents has a markedly remedial effect. I need refer only to the use of iodine and intramine in tuberculosis, chronic ulcus molle, and to chronic gonorrhœa.

The bigger the size of the molecule and the greater its adsorptive capacity, the more easily will a drug like salvarsan be adsorbed, and the more readily will the adsorbed compound break down. When the lipoid-globulin molecules first break down the area of their action is widened; hence the catalytic action of the arsenic will have its fullest play. If salvarsan became attached to small molecules, the adsorbed compound would not break down; at all events, not until much later than it does in the case of syphilis. Moreover, as much of the arsenic compound would not be adsorbed, this would mean that the arsenic would get little chance of acting as a catalyst. Therefore, salvarsan seems to act especially in protozoal diseases because of the physical state of the lipoid-globulin molecules of the serum, and it fails to act as a bactericidal agent because the lipoid-globulin molecules in the serum of bacterial diseases do not possess the requisite physical properties. From the fact that Ehrlich noticed that it was only such organisms as the *Spirochæta pallida,* the spirillum of recurrent fever, and the trypanosome which were killed by the action of salvarsan *in vitro*, two important deductions may be made:

(1) that the spirillum of recurrent fever and the trypanosome are killed because of the free hydroxyl groups their molecules contain; (2) that the trypanosome is not the sole cause of sleeping-sickness.

To sum up the points which stand out, we can briefly say that strongly adsorbed metallic and non-metallic compounds become attached to the lipoid-globulin molecules of the syphilitic parasite, the plasma cells, and the serum, by virtue of their amino groups and of the peculiar physical properties of the protozoal lipoid-globulin molecules. The metallic compounds attack those phases of the *Leucocytozoon syphilidis* in which reaction is most marked, especially the spirochætal phase, in virtue of its free hydroxyl groups. Both metals and non-metals act as catalysts, that is to say, they accelerate the complementary or oxidase-reducase action of the lipoid-globulin molecules of the serum and of the plasma cells by increasing directly and indirectly the supply of active oxygen, which is necessary for the action of adsorption—a chemico-physical action which destroys the parasites.

RESEARCH IN CHEMOTHERAPY.

If salvarsan be compared with atoxyl and arsacetin, it will be seen that in salvarsan the arsenic is trivalent, while in atoxyl and arsacetin it is pentavalent. Arsenic in a pentavalent state is less active in exerting its therapeutic influence on protozoa than when it is in a trivalent state. This is due to the fact that, in a molecule in which all the valencies are satisfied, the influence desired is less likely to act than when some of the valencies are unsatisfied. In this connection, Hardy's rule is an important one to bear in mind—viz. that the precipitating power of an electrolyte depends upon the valency of the ion. From this it is clear that no compound of a univalent ion would be likely to have a therapeutic action at all akin to that of salvarsan. Therefore, so far as future research is concerned, the element employed should at least be a di- or, better, a trivalent ion.

Apart from valency, two other considerations present themselves: (1) The degree of adsorption of the compound; (2) the atomic weight of the element.

It is a well-known fact that a strongly adsorbed organic anion, such as salicylic acid, is more powerful in precipitating aluminium hydroxide than a weakly adsorbed univalent inorganic ion. Hence to obtain the best therapeutic action with a compound, we see that it must be organic, and the more strongly adsorbed it is the better, the reason being that a ratio exists between the strength of adsorption of the compound and the power it has in diminishing the mechanical surface energy. It is now clear why salvarsan should be so much more effective than arseno-phenyl-glycine, arsacetin, or atoxyl. It is also a well-known fact that, in the precipitation of a negative colloid by kations, those of the heavy metals and of organic bases are more active than would be expected from their valency, and that this is to be accounted for by the fact of their great mechanical adsorption. This shows us, then, not only why mercury should be useful in syphilis, but also why it should be toxic. Owing to the great mechanical adsorption exerted by the heavy metals, it is at once obvious that strongly adsorbed organic compounds of them would be too toxic for injection.

Studying the rationale of chemotherapy in this way, one may be saved from doing an amount of useless experimental work by excluding all univalent and divalent elements, as well as all those elements which have high atomic weights.

Seeing that arsenic, a trivalent element in the form of a di-oxy-di-amino-benzene compound, may be toxic, the atomic weight being only 75, and that the corresponding compound of antimony, di-oxy-di-amino-stibino-benzene is more toxic still, the difference in the atomic weight being $120 - 75 = 45$, it is perfectly clear that, if we wish to find a non-toxic compound, we shall have to seek for elements which are trivalent with a smaller atomic weight.

Before mentioning the elements I tried there are one or two other points to be considered.

Di-oxy-di-amino-stibino-benzene is not only more toxic than its corresponding arsenic compound, but its therapeutic action is infinitely less. Comparing the two bodies we find that the arsenic in salvarsan is both metallic and non-metallic, while in the antimony compound just mentioned the antimony is entirely metallic. It therefore struck me that a less metallic element than arsenic might prove to be its therapeutic superior; in any case the probability was great that it would be considerably less toxic.

Salvarsan is a strong oxidising body; indeed, its arsenic acts catalytically as a peroxidase, but at the same time it is a reducing agent, although its properties in this direction are probably not made use of in the body. This led me to think that a body similar to salvarsan, which had stronger reducing properties, would probably do just what salvarsan failed to do.

I wanted, then, an element which had the following properties: (1) of more than one valency; (2) an atomic weight of less than 75; (3) a non-metal; (4) a reducing agent.

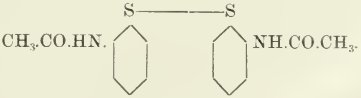
Only two elements occurred to me which would fulfil these conditions, and they were phosphorus and sulphur. I discarded phosphorus, owing to the fact that it can produce very toxic symptoms, such as fatty degeneration of the liver, so I conducted experiments with sulphur and succeeded in making a compound which has in some respects a more powerful therapeutic action than that of salvarsan. I prepared several compounds, but soon found that one was much superior to the others, and this one was di-ortho-amino-thio-benzene, or "intramine," as it is called for short.

Further research showed me that it was highly probable that other metallic compounds could be found which would prove to be as efficacious as and less toxic than salvarsan. Seeing that the metal must be trivalent and not of high atomic weight, I began to experiment with iron, manganese, and aluminium. In a short time I was able to prepare some compounds of iron and aluminium, which turned out to be non-toxic and to have a marked therapeutic action like salvarsan, if used in sufficient and repeated doses.

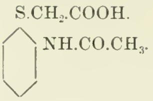
NON-METALLIC COMPOUNDS.

Sulphur.

I prepared two basic and two acid compounds. The first acid compound was the acetyl derivate of di-ortho-amino-thio-benzene, and the second acid compound was the condensation product of the base with mono-chloracetic acid.

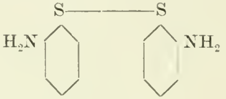


Acetyl derivative of intramine.

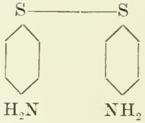


Condensation product with mono-chloracetic acid.

These two products may be quickly dismissed, as both were extremely painful when injected intramuscularly, and their therapeutic action was practically *nil*, which was to be expected, since the amino-groups have been interfered with. The two basic compounds prepared were di-para-amino-thio-benzene and di-ortho-amino-thio-benzene. As the therapeutic action of the first-mentioned drug was not as good as that of the second, it was discarded.



Di-ortho-amino-thio-benzene (intramine).



Di-para-amino-thio-benzene.

Intramine is absolutely non-toxic; consequently, any dose may be employed, and it may be repeated as often as is thought necessary. The usual dose I employ for an adult is 1 grm., this quantity being suspended in 9 c.c. of olive oil or liquid paraffin and injected intramuscularly.

Intramine does not oxidise on exposure to air, therefore the unused contents of a phial need not be thrown away, and a wide-mouthed bottle containing several grammes may be kept and used like mercurial cream. The pain caused by the injection, when 0·5 to 1·0 grm. or more is employed, usually renders the patient *hors de combat* for two or three days. Unfortunately, this cannot be entirely avoided.* A few days later an erythema may appear over the injected area, which remains localised or spreads over the body, but in all cases it disappears in a day or two. The great point in favour of intramine is that, however severe be the local reaction, it rapidly becomes absorbed and never leaves any induration behind it, provided no quinine and urea hydrochloride are mixed with it, and that it is injected into the gluteus medius muscle.

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* This disadvantage has now been overcome.

When compared with salvarsan, I soon found that in the primary and generalisation stages salvarsan was superior to intramine, but that in the recurrent stages the opposite was the case.

Further experiments showed me that, in the early stages of syphilis, previous administration of a metallic compound greatly increased the action of intramine, but that in the recurrent and late stages the intramine increased the action of the metallic compounds.

Before describing the metallic compounds I prepared, it will be as well to discuss the mode of action of intramine in further detail. Having already made some allusions to the *modus operandi* of intramine, to save recapitulation I will begin with its action in the oxidase-reducase system. The oxidase-reducase system can be expressed in short as the hydroxyl-hydrogen system of the internal phase. The metallic ion becomes attached on to the hydroxyl group; normally, the metal is iron; when salvarsan is injected it is arsenic, etc. This metallic hydroxide combines with hydrogen ions and hydroxyl ions in the form of hydrogen peroxide to form active oxygen, as shown by the following diagrammatic equation:

$$R.Fe(OH)_3 + 5H + 2H_2O_2 = R.Fe + 6H_2O + O''$$

The iron-protein which is formed as the result of the reaction soon becomes reconverted into iron hydroxide-protein, as in the following diagrammatic equation:

$$R.Fe + 4H_2O = R.Fe(OH)_3 + 4H + OH.$$

When intramine gets into the body, the compound presumably breaks down at the link between the two sulphur atoms. The sulphur then forms disulphide-protein, which reacts with the hydrogen and hydroxyl ions of the external phase to form sulphur-protein, mercaptan-protein, hydroxyl ions in the form of hydrogen peroxide, and active hydrogen, as indicated by this diagrammatic equation:

$$R.S.S.R. + 2H + 4OH = R.S. + R.SH + 2H_2O_2 + H^{\cdot}$$

In this way two molecules of peroxide of hydrogen are formed, exactly the amount required for the metallic hydroxide to act upon in order to form active oxygen.

Metals, then, form active oxygen directly, and non-metals do so indirectly.

The mercaptan-protein is able to combine with any free sulphur to form hydrogen sulphide and disulphide-protein, as in the following equation:

$$2R.SH + S = H_2S + R.S.S.R.$$

The mercaptan-protein is also able to combine with any free oxygen to form water and disulphide-protein, as in this equation:

$$2R.SH + O = R.S.S.R. + H_2O.$$

Adding the knowledge just obtained to that gained by clinical observation, further light is thrown upon the affinity of mercaptan-protein for oxygen. If the mercaptan group becomes oxidised by the active oxygen present, there will be less active oxygen resulting from the oxidising action of the metallic hydroxide; hence, if intramine be given first and salvarsan afterwards in early syphilis, when the greatest quantity of active oxygen is present, one would expect that those phases of the *Leucocytozoon syphilidis* which are most easily killed by oxidation would be able to flourish, that the customary therapeutic action of salvarsan would not be witnessed, and that the symptoms might even be temporarily aggravated. This is exactly what happens clinically. The spirochætæ are not killed quickly by intramine, and, if salvarsan is given directly afterwards, it appears to have no immediate influence on the symptoms.

If the metallic compounds are allowed their full play first, as the catalysts of the oxidase system, the introduction subsequently of a strong reducing agent, like intramine, in virtue of its action, sets free sufficient peroxide to be subsequently converted into active oxygen by the metallic compounds, thereby preventing the adverse action of the mercaptan-protein. This being the case, one would expect that the phases of the *Leucocytozoon syphilidis* would be quickly vanquished, and that the symptoms of the disease would rapidly disappear. Once again this is exactly what happens clinically.

If metallic compounds be first administered in early syphilis, the spirochætæ are killed at once and the symptoms improve. If intramine be now injected, some of the other phases are killed immediately, and the symptoms vanish at a very much quicker rate than they otherwise would have done. I need only cite one case to show the truth of this :

Case 1.—A patient had a typical Hunterian chancre in the corona ; there was a moderate loss of surface, and the sore was markedly indurated. I gave an intravenous injection of galyl (40 cgrm.), and three days later an intramuscular injection of intramine (3 grm.). There was practically no change in the chancre when the intramine was given, but a few days later not only had the sore completely healed, but the induration had entirely vanished.

I have seen severe papular syphilides, scarcely influenced by galyl alone, as the following case shows, disappear in a few days when intramine was injected :

Case 2. — The patient had a primary sore in the corona, hard infiltrative œdema of the whole of the penis, and a generalised papular syphilitic eruption. No improvement followed three intravenous injections of galyl; instead, more papules appeared. Within ten days after one injection of intramine every lesion had vanished.

In the recurrent and late stages of syphilis, the exact opposite to what has just been said would be expected, since in these stages the reducing action of the resisting substance is more powerful than the oxidising action. One case will suffice to prove this :

Case 3.—A patient had a gumma which encircled the corona and spread on the under surface of the penis on to the scrotum. In less than one week after receiving only one intramuscular injection of intramine (2 grm.) the ulceration had completely healed. If this case had been treated with salvarsan alone it would have taken about three weeks for the sores to have healed up, and during this time it would have been necessary to have given two or three intravenous injections.

I have treated with immediate success by intramine late syphilitic lesions which had remained practically uninfluenced by salvarsan, with mercury and iodides subsequently. I must cite a case which bears this out to the letter :

Case 4.—A man, aged 70, had syphilitic glossitis for twenty-five years. Eighteen months before he was given intramine he had two intravenous injections of salvarsan, and these were followed by three courses of mercury and iodides, with practically no improvement in the clinical condition. When an intramuscular injection of intramine was prescribed (2 grm.) the tongue exhibited the following features : There was an ulcer in the centre about the size of a sixpence, with a lateral fissure running from it on both sides. Just posterior to the ulcer a hard wart was situated. The movements of the tongue were impeded and very painful. In a few weeks after the injection the ulcer had completely healed, the fissures and wart had vanished, the natural movements of the tongue and its suppleness had returned, and, in the words of the patient, "my tongue has never been so well as long as I can remember."*

Iodine.

While on the subject of reducing agents, I might as well explain how iodine acts. Iodine has a more marked therapeutic action in late than in early cases of syphilis for the same reason that intramine has. Like intramine, iodine adsorbs hydrogen- and hydroxyl ions to form peroxide for the oxidase system, as in the following diagrammatic equation :

$$4I + 5H + 4OH = 4HI + 2H_2O_2 + H^{\cdot}$$

The preparation of organic compounds of iodine, possessing a therapeutic action at all akin to intramine, is impossible, owing to the fact that iodine is a monovalent element. Iodine increases the action of intramine, presumably because it is readily adsorbed by a mercaptan group, thus checking the deleterious action of this group. The following formula shows the interaction :

$$2R.SH + 2I = R.S.S.R. + 2HI.$$

Therefore, when prescribing intramine, I usually order iodine beforehand. To obtain the maximum effect with iodine, it is best to give intravenous injections of colloidal iodine. Colloidal iodine can also be injected intramuscularly, and it can even be taken internally. Colloidal iodine has none of the disadvantages of the potassium salt, it is not depressing, and patients do not show an idiosyncrasy towards it. Almost any quantity can be injected intravenously and as often as is considered necessary. I usually inject 100 c.c. to 200 c.c. of collosol iodine, which contains 1 in 500 of Crookes's colloidal iodine.

METALLIC COMPOUNDS.

Iron.

As iron seemed to me to be the natural peroxidase, and having obtained such good results with intramine, a drug which increases the natural perhydridase, I anticipated good results from the use of an organic iron compound, and my anticipations have fortunately in part been realised. The iron bodies prepared were the para-amino-di-hydroxy-ferric-benzene sulphonate, the di-para-amino-hydroxy-ferric-benzene sulphonate, and the tri-para-amino-ferric-benzene sulphonate, the formulæ of which are as follow:

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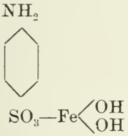
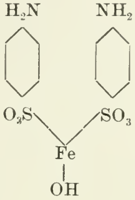
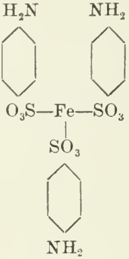
* A year has now passed since the intramine was injected, and, in spite of the fact that no other treatment has been prescribed, the tongue condition has never once gone back.



Para-amino-di-hydroxy-ferric-benzene sulphonate.



Di-para-amino-hydroxy-ferric-benzene sulphonate.



Tri-para-amino-ferric-benzene sulphonate.

Of the three compounds just mentioned, the tri-para body appears to be the most suitable. It is a crystalline body, soluble in water, to which it imparts a deep orange colour. Ferrivine, as this compound is commercially called, is non-toxic, and it is supplied as a 1 per cent. solution—*i. e.* 100 c.c., or 3·5 oz., contains 1 grm. of the salt. The solution is stable, it does not oxidise in the air, and if desired it can be diluted with distilled water. The dose suggested may be repeated without risk at frequent intervals. The dose I usually employ is 1 grm., but I have injected 2 grm. or 3 grm. The only disadvantage which I have so far experienced with big doses of ferrivine is that the patient sometimes feels faint after the injection. Recovery sets in in a few minutes, when the patient can do as he likes. Occasionally typical shock or collapse immediately follows the injection, due to a temporary upset of the normal hydrogen ion concentration of the serum. I am in the midst of experiments in the hope of overcoming this disadvantage, the results of which up to the present point to success.*

PRACTICE OF CHEMOTHERAPY.

It would be as well now to give a sketch of the clinical value of these new drugs, and to state how they should be used with the already known remedies in the treatment of syphilis.

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* While correcting these proofs I am able to say that the disadvantage has been entirely overcome.

Ferrivine acts like salvarsan, and, owing to its non-toxicity, larger doses can be given, which may be repeated at shorter intervals, even daily. Generally speaking, the symptoms of primary and generalised syphilis disappear within four days after the second or third intravenous injection. Induration in chancres and those dense, infiltrated, brownish papules are about as resistant to ferrivine as they are to salvarsan; but if intramine be prescribed aftĕr the second or third injection, the hardest induration and the most resistant papule will vanish within a fortnight. Owing to the iron not being in a sufficiently adsorbed condition, its therapeutic action is not regular. Experiments are in hand to prepare a more strongly adsorbed iron compound.

In the recurrent and late stages of syphilis, intramine should always be prescribed first, when the symptoms vanish in a few days. In cases of cerebro-spinal meningitis the pains disappear within twenty-four hours; in degenerative myelitis the subjective symptoms are often improved, and I have also seen considerable benefit follow intramine in cases of degenerative encephalitis.

I will describe a case of degenerative encephalitis treated with intramine, as it shows so well what can be done by combining reducing and oxidising remedies:

Case 5.—The patient was suffering from the depressive type of degenerative encephalitis; he showed no change of facial expression; would not speak; he had no control over his sphincters; and was at times violent. I prescribed two intramuscular injections of intramine with the most extraordinary improvement—the facial expression returned within a few days and the patient entered into conversation. Hoping that the condition might be still further improved, a third injection was given, with the result that the patient became worse than he had ever been. I had suggested that after the second injection of intramine a metallic compound should be administered, but as the medical man in attendance wished to see what intramine alone would do it was not prescribed. Seeing that the patient had become worse after the third injection, which was what I expected, I hazarded the opinion that if a metallic compound were given now his improvement would be sudden and greater than on the first occasion. An intravenous injection of galyl was administered, with the result that in forty-eight hours' time the patient became a rational individual. For how long the improvement is going to be maintained I cannot say, but this case is especially interesting to me as a proof of my theory of oxidation and reduction. More than two months have elapsed since the patient had his last injection, and a steady improvement has been maintained. The patient has now returned to his business. Before he came under treatment he could not write.

I have had two other cases in which as marked an improvement has been obtained. With salvarsan I have seldom seen a case of degenerative encephalitis improve, and I have seen many get worse.

Just as the maximum therapeutic action is obtained in early syphilis if intramine follows the administration of aluvine or ferrivine, so is it the case if in late syphilis one or other of the metallic compounds follow intramine. I have treated some cases of cerebrospinal meningitis first with an intramuscular injection of intramine, then with two intravenous injections of a metallic compound, and, finally, with mercury and iodides, with the very greatest success; so much so that I think such patients are better advised to have the treatment just outlined in preference to intraspinal injections of salvarsanised serum. Owing to the non-toxicity of intramine and ferrivine, serum withdrawn after their administration and injected intraspinally has a most beneficial influence upon central nervous lesions, superior to that of salvarsanised serum, and, moreover, no toxic symptoms occur, as are too often witnessed when galyl and the other arsenical substitutes are used. The following case is one in point:

Case 6.—A man, aged 34 years, came to me complaining of double vision. He had contracted syphilis five years previously, and had been treated thoroughly with mercurial inunctions and injections before the symptoms of the generalisation stage manifested themselves. The patient also had nine intravenous injections of salvarsan at various periods, but had never had another symptom of syphilis. On examination, I found that there was a unilateral partial third nerve paralysis, the pupils were unequal, and the reflexes were sluggish. The patient had no knee-jerks, and there were areas of diminished tactile sensation. I elicited from the patient that he had lost much weight and that all sexual desire had vanished in the last few months. I gave him three intramuscular injections of intramine, alternating them with three intravenous injections of aluvine. After each injection I gave an intraspinal injection of the prepared serum. The cerebrospinal fluid when first examined exhibited the typical features of degenerative myelitis; after the fifth injection it was practically normal, and by this time all the objective and subjective symptoms had vanished. The double vision disappeared after the first injection of intramine, showing clearly that the cranial nerve lesions in degenerative myelitis must be of meningeal origin, commencing in the meninges covering the nuclei in the base of the brain.

I have recently had a case of degenerative myelitis, the chief symptom being that the patient could not walk without the aid of a stick. After one intramuscular injection of intramine and two intravenous injections of ferrivine, the gait so improved that the patient was able to walk without a stick.

Interstitial keratitis, a lesion uninfluenced by salvarsan, clears up at once in a most marvellous way with intramine. In those not immediately improved mercury has acted beneficially afterwards.

In outlining the treatment I now adopt in the various stages of syphilis, there are two very important questions which arise, the correct answers to which it is necessary to find, in order that we may treat our patients in the best way possible:

(1) Assuming that in the doses given the oxidising effect of salvarsan and ferrivine is equal, is that effect going to be enhanced by giving an injection of each, or is the effect going to be the same if three injections of either one are prescribed? Theoretically, I should doubt whether any difference in effect would be produced, but whether this is the case practically, remains to be seen—a point by no means easy to determine.

(2) If we fail in curing a case of syphilis at once, are we right in continuing treatment after the disappearance of the symptoms, or might it not be better for the patient to be treated only symptomatically?

The syphilitic parasites are attacked first and foremost by the resisting substance—*i. e.* the lipoid-globulin molecules in the serum. The resisting substance has an oxidising and reducing action, actions which we increase by salvarsan and ferrivine, on the one hand, and by intramine and iodine on the other.

An increase in size of the lipoid-globulin molecules, produced by the administration of the synthetic remedies just mentioned, results in a breaking down of the molecules, ultimately with a diminution in the amount of the resisting substance. Therefore, the continued administration of powerful oxidising and reducing remedies might possibly be expected to result in so little of the compound being adsorbed that their oxidising and reducing actions would be reduced perhaps to *nil.* Seeing that both oxidation and reduction are catalytic reactions, it might be possible theoretically that only the minutest traces of the metallic hydroxide and the disulphide are necessary to continue the good work. Since mercury acts mechanically and probably not as a peroxide at all, and considering that its action is entirely dependent upon the size and adsorptive capacity of the lipoid-globulin molecules, it might be assumed theoretically again that the administration of mercury, once the properties of the resisting substance have been reduced, would be entirely superfluous.

Ever since the advent of salvarsan, I have been struck by the large increase of cases of meningeal syphilis, and the very frequent occurrence of lesions, in spite of the fact that the patient was well under the influence of mercury. I have also seen many cases in the latent stage precipitated into a condition of degenerative myelitis and degenerative encephalitis by the administration of our powerful remedies. So far as dealing with patients in the latent stage is concerned, I have for some time made up my mind never to prescribe treatment if after a thorough clinical examination I found no symptom. I have also long since made up my mind to treat symptomatically only those patients who have once entered the recurrent stage; but as to how a case in the generalisation stage should be best treated, a little further discussion is necessary.

To make the subject clear, I will picture the body as consisting of two parts: (1) the systemic part; (2) the nervous. The nervous part is largely dependent upon the systemic part for its resisting substance.

If the resisting substance in the systemic part has been reduced by treatment, spores which are resistant to treatment may possibly be prevented from developing if small doses of the remedies are continually being prescribed. The rule is far from being invariable. Against this, one must consider the frequency of recurrences when mercury and iodides are not prescribed after a course of several injections of salvarsan, and how the protective action of mercury and iodides compares with that of the resisting substance when working alone.

Systematic recurrences are far more common when salvarsan is not followed by mercury and iodides, but the frequency of the same and as to when they appear depend upon the number of injections given. If three or less injections of salvarsan are given, the recurrences are more frequent than when six or more injections are given in one course of treatment, but they appear much later. Usually, twelve or eighteen months have elapsed before they make their appearance, while, after a course of several injections, a recurrence may appear in two or three months. Unless the individual has the opportunity of observing many cases, this somewhat paradoxical result may easily lead to false conclusions being made.

The explanation of this disparity as to the time at which the recurrences appear is as follows: When three injections of salvarsan are prescribed, the resisting substance is scarcely reduced, with the result that it continues exerting its power until the parasites ultimately get the upper hand, which is hardly ever under twelve months. When several injections have been administered, the resisting substance is so reduced that the spores which have not been killed by the treatment will be able to develop on a soil which is the same to them as a new soil; consequently, symptoms will appear after the usual incubation period; therefore, two or three months later.

The early syphilitic lesions are far less dangerous, and cause much less local damage, than late syphilitic lesions; hence the systemic recurrences, after a course of several injections, are preferable to those which occur when only three injections have been made, since the former produce fewer degenerative changes, especially in the vessels, which in most lesions are primarily attacked.

Therefore, a course of several injections produces better results than a course of a few injections, and since the recurrences after both are fewer in number when the injections are followed by mercury and iodides, these two drugs should not be omitted in the treatment of syphilis.

As mercury and iodides can have such an infinitesimal action when the resisting substance is reduced, might it not be better for the patient after a course of several injections to wait eight to twelve weeks before taking mercury? Eight to twelve weeks is about the time the resisting substance takes to get back to its normal state. Now mercury and iodides have nothing like the influence in altering the state of the resisting substance that the strongly adsorbed compounds possess, and since both may have some power in preventing the spore from developing, it would seem wiser not to allow any interval to elapse between stopping the synthetic metallic compounds and commencing the mercury.

A question which is impossible to answer is how long the mercurial treatment should be maintained. A correct answer could only be given if we knew that a spore would not develop if it had been dormant for a certain number of years. A spore may remain dormant for fifty years, and then redevelop and cause symptoms. Therefore a definite answer will never be forthcoming. Furthermore, we do not know what influence treatment has upon dormant spores, nor do we know whether treatment postpones their recrudescence. In this uncertainty it is best to let our clinical experience guide us, and to give one year's treatment when the case of syphilis is in the primary stage, and two years' treatment in the generalisation stage.

Owing to the fact that the nervous part is dependent for its protective substance upon the systemic part, it will be readily understood that if the organisms have reached the nervous part before treatment has commenced, they will be able to develop therein the more readily the quicker the resisting substance in the systemic part has been reduced, provided at the same time the organisms in the nervous part are not vanquished by the treatment.

It will follow, therefore, that the incidence of cerebro-spinal meningitis will be greater when many injections of salvarsan have been prescribed than when a few, since it is difficult in every case to make injections sufficient to kill the organisms in the nervous part. Cerebro-spinal meningitis is a curable condition, and, moreover, its occurrence practically precludes the patient from getting a degenerative lesion later.

Now let us consider what happens to the nervous part if only a few injections of salvarsan are administered. The resisting substance is not strong enough to kill the parasites, but strong enough to prevent them developing sufficiently to produce symptoms. In this state, the spores can and do migrate into nerve tissue proper, where they meet with still less resistance, with the result that now any symptoms which appear will be degenerative in character, and, therefore, more or less incurable. Once again we see that a course of several injections is preferable to a course of only a few.

The onset of nervous lesions is naturally dependent upon the number of organisms that reach the meninges before treatment is begun. Cerebro-spinal meningitis is much more common in patients, who have severe generalised symptoms than in those in whom the so-called "secondaries" are slight. For all practical purposes, it may be said that a ratio exists between the severity of the early cutaneous eruptions and the occurrence of early cerebro-spinal meningitis. As the symptoms of cerebro-spinal meningitis almost invariably occur between eight and twelve weeks after the last injection of salvarsan, it is wise to give every patient in the generalisation stage an extra course of powerful treatment round about this time.

What effect the introduction of intramine is going to have upon the points just raised I am not in a position yet to say, but one thing is clear—namely, that the administration of intramine reduces the number of the long course of the metallic compounds by about half, and increases the result produced.

In the primary stage I prescribe first of all collosol iodine and inject intravenously a large dose of a metallic compound, which I repeat one or two days later. Three days after the second injection I give an intramuscular injection of intramine (1 grm. to 2 grm.), and between the fourth and seventh day after, I inject intravenously another maximum dose of a metallic compound, and continue mercury, intramine, and iodides for one year, as follows:

(1) Eight fortnightly intramuscular injections of grey oil, 2 gr. to 3 gr. of mercury.

(2) Eight fortnightly intramuscular injections of intramine, 1 c.c. to 3 c.c.; mercury and intramine alternately. By injecting mercury and intramine alternately, the former is prevented from producing salivation, tender gums, and local accumulations in the muscles.

(3) One month in every three, collosol iodine should be prescribed. The first month of iodine should be commenced after four doses each of mercury and intramine have been injected.

(4) One month's rest should follow every eight injections each of mercury and intramine.

In the generalisation stage, I prescribe collosol iodine at once, and two or three intravenous injections of a metallic compound both before and after one or two intramuscular injections of intramine, allowing two days to intervene between each intravenous injection. I then give four courses of the mixed mercury, intramine and iodine treatment, and, two months after the last intravenous injection, I inject intravenously a maximum dose of a metallic compound before and after a large intramuscular injection of intramine.

In all recurrent and late cases I give first of all one or two intramuscular injections of intramine, then one or two intravenous injections of a metallic compound, and follow up the same with one course of the mixed treatment. This treatment will also do for cases of non-degenerative meningo-encephalitis and myelitis. In cases of degenerative encephalitis and myelitis, in which more drastic treatment might be expected to give more satisfactory results, I make the following:

(1) An intramuscular injection of intramine.

(2) Four days later, an intraspinal injection of prepared serum which has been drawn off on the third day.

(3) Three or four days later, an intravenous injection of a metallic compound. The metallic compound should not be galyl, kharsivan, neo-kharsivan, or any of the other French substitution products for salvarsan, as they are too toxic.

(4) Three days later, an intraspinal injection of prepared serum, which has been collected the day before.

The injections of the non-metallic and metallic compounds should be continued alternately, until the cerebro-spinal fluid is normal or closely approaching the normal.

Women who are pregnant should be treated as first described under the heading of the generalisation stage, and two courses of the mixed treatment should be given without any pause between. Extra injections at the second month are unnecessary.

Congenital syphilitics should have the mixed treatment for two years, with the exception that the mercury should be administered *per os* and continuously. All recurrent symptoms should be treated symptomatically and intravenous injections prescribed if practicable, as suggested in recurrent and late cases of acquired syphilis.

Although I have not yet used ferrivine on quite such a large scale as intramine, I have made sufficient injections to state the fact that the need for the use of a toxic metal like arsenic will, it is hoped, soon no longer remain. Ferrivine is in some cases superior to salvarsan: I had under treatment a man with three chancres on the penis; ferrivine was injected on a Tuesday, and by the following Saturday the sores had healed; in other cases it is certainly inferior. The drug is non-toxic; consequently, bigger doses may be given, and they may be repeated at shorter intervals.

Ferrivine can be improved upon, and I am now undertaking experiments with that end in view. I am confident that in time an iron compound will be prepared which will be in every way superior to salvarsan.

So far as the oxidising agents are concerned, there is nothing further to be said; but as regards the reducing agent, intramine, I must say a few more words, as its introduction into our therapeutic armamentarium is going to have not only a very marked effect in combating protozoal diseases, but also all chronic infections.

No drug so far known has had much effect upon lupus. Dr. Adamson has treated five cases with intramine with the most striking results, even after only one injection. All ulcerative areas heal up in a few days, and the large granulomatous masses become flush with the surrounding surface. As to whether intramine only temporarily benefits lupus or cures it, the future will show. Chronic ulcers of the leg, which have been treated for years without improvement, immediately begin to mend when intramine is injected. Intramine is useful in chronic gonorrhœa, and it possesses very strong antiseptic properties. It is just possible that intramine may have a place in the treatment of malignant disease, and it is practically certain that in leprosy it will prove invaluable.

Before closing, I must refer to one or two other points which are not only of practical interest, but which also strongly support my oxidation-reduction theory.

Chilblains probably arise owing to insufficient oxygenation of the tissues in the extremities. If this be true, metallic compounds applied locally to the particles should relieve the condition. The metallic compounds must be in the colloidal form, because with friction and the Brownian movement of the particles, it is possible to get some of the particles into the tissues. If colloidal silver (*collosol argentum*) be rubbed into the chilblains, one application is sufficient to get rid of them. I have treated two bad cases in this way with marked success.

Colloidal silver in the form of suppositories has also a beneficial action on piles, because the Brownian movement of the silver particles still continues, even in the depth of the gelatin with which the suppositories are made.

If fresh or acute ulcers are examined microscopically and stained with pyronin and methyl green, it will be noticed that nuclei predominate, and that the whole section looks as if it has only taken the methyl green. Methyl green is avid for active oxygen; hence it is clear that the cells in acute ulcers are rich in active oxygen. Applications of colloidal metallic compounds to such ulcers greatly accelerate their healing. If chronic ulcers are treated in the same way, the avidity of the cells for pyronin is as marked as was the avidity for methyl green in the previous case. Pyronin stains reducing foci, as it exhibits a strong affinity for the peroxide. Applications of colloidal non-metallic compounds cause such ulcers to heal immediately. One application of intramine to a chronic soft sore which had persisted for two months healed it in forty-eight hours.

I have treated other chronic ulcers with intramine with the most extraordinary results. The action of intramine is much more rapid than that of scarlet red, and I should imagine it will prove of much greater value than the Simpson light. Another great advantage possessed by intramine when applied locally is that it causes a great accumulation of lymph around the area affected. Owing to its lymphagogue action, intramine might possibly prove useful in the treatment of old bullet and shrapnel wounds.

Conclusion.

The theory that diseases are combated by drugs which simply increase the amount of oxygen directly or indirectly is, I think, fully proved, with the result that treatment is now put upon a logical basis and empiricism is removed. The paths opened up for future research are infinite, the treading of which must always lead to some substantial progress being made, and not to a further penetration into darkness, the direction taken by so much of the research work done in medicine in recent years.

The theory of oxidation and reduction has not only explained directly the *modus operandi* of chemotherapy, but also indirectly that of immunity, with the result that the rationale of dyeing and staining, of the immunity reactions, and of anaphylaxis is rendered clear. We should now be able to discard the hundreds of coined words which have never served a useful purpose, and to replace irrational by rational tests.

Further details of the subjects referred to will be found in my Hunterian Lectures.*

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* *Links in a Chain of Research on Syphilis* (*Oxidation and Reduction*), Harrison.

DISCUSSION.

Prof. W. M. **BAYLISS**, F.R.S.: This paper is one that contains much important and suggestive matter, but is very difficult to criticise. I find in the physico-chemical hypothesis much that conveys no very definite meaning to me. while the statements appear to be contrary to the knowledge which we possess. To begin with, I think it unfortunate that the phenomena of oxidation and reduction should happen to form the basis of the main thesis. Although these phenomena are undoubtedly of the greatest importance. their mechanism in the living cell is, as yet. one of the most obscure in the whole of physiology. There are. indeed, enzymes which result in the production of active oxygen and active hydrogen respectively. but we do not yet know precisely what these agents are. Again. while. of course, any oxidation of one substance is accompanied by the reduction of another, the same substance cannot be oxidised and reduced at the same time. as seems to be implied in the author's conception of a lipoid-globulin as an oxidase-reducase system. But I admit that I have possibly misunderstood the statement. There is no evidence, so far as I am aware, that oxygen has any necessary connection with adsorption, which is purely a result of molecular forces at boundary surfaces. The possibility of a lipoid-globulin must be admitted, but I fail to find any experimental evidence brought forward to show that it plays any part in the phenomena of chemotherapy. The phrase "permeability of molecules" conveys no meaning to me. When a membrane is permeable to a particular substance, this substance is not supposed to pass through the molecules of the membrane, but between them. Again. I fail to grasp how the valency of an element can play the part assigned to it. The peculiarity of an organo-metallic compound is that it is not electrolytically dissociated. Hence electrically charged ions are not concerned in its activity. It seems rather more probable that the properties of the metal itself are required. and that the function of the organic part of the molecule is to bring it into close relation with some constituent of the cell, but not necessarily by means of special receptive molecular groupings. Why arsenic should have so powerful a toxic action is almost as impossible to say at present as why its chemical properties differ from those of lead or zinc. I should like to say in conclusion that any doubts expressed as to the validity of the theoretical basis of the author's treatment of syphilis do not necessarily detract from its possible practical value, the importance of which requires the most careful testing.

Dr. C. H. **BROWNING**: I desire to associate myself with the views expressed by Prof. Bayliss in regard to the highly speculative discussions in Mr. McDonagh's communication. Prof. Bayliss is universally recognised as one of the leading authorities on the chemistry of those processes which Mr. McDonagh invokes in order to form a basis for his chemotherapy; accordingly one must attach the greatest weight to Prof. Bayliss's expression of opinion on the theories advanced by the author of to-night's communication. However useful such lines of thought may have been to Mr. McDonagh himself. I doubt whether. in their present phase and without rigid experimental proof. they will contribute materially to the understanding of the subject by others. These considerations. however, do not detract from the therapeutic results. which are of outstanding interest. To be able to clear up, with certainty and rapidity, the lesion of interstitial keratitis in congenital syphilis is an achievement of the first magnitude. It is highly interesting that Mr. McDonagh should have attained this success with an organic sulphur compound which has been known for a very long time—upwards of thirty years. As regards the question of the relationship of chemical constitution to therapeutic action, it is a striking confirmation, to my mind, of the general soundness of Ehrlich's work that this sulphur compound which, in its molecular configuration, bears so close a resemblance to salvarsan, with sulphur substituted for arsenic atoms, should likewise exert a marked action on syphilis. With regard to Mr. McDonagh's opening remarks on the rationale of chemotherapy, I desire to draw attention to a grave misapprehension which might arise in the mind of readers. Ehrlich, to whom all subsequent workers in this domain must remain for ever indebted, did not, to begin with, devote his attention exclusively, or even principally, to the investigation of arsenical compounds. The curative action of the non-arsenical, sulphur-containing dye, methylene blue, in malaria was his first observation, and the discovery of trypan-red, also a non-arsenical substance, marked the commencement of the systematic investigation into synthetic antiparasitic drugs. It was only after the therapeutic action of the organic arsenical compound, atoxyl, had been demonstrated by Thomas and Breinl, of the Liverpool School of Tropical Medicine, that Ehrlich concentrated his attention on the investigation of this group of arsenical derivatives. Salvarsan was the logical outcome, but the logic was that of genius. That salvarsan does not by any means mark the culminating point of this work is proved, *inter alia*, by to-day's communication. That arsenical compounds did not, even for Ehrlich, constitute the acme of chemotherapy is shown by the potent non-arsenical, acridin derivative "trypaflavin," which was synthetised under his guidance, and also by one of his latest discoveries, the complex copper-salvarsan compound, the work on which was interrupted by his death. His experiments showed this compound to be many times more active than salvarsan itself in trypanosome infections.

Dr. F. H. TEALE: I ask, what evidence has Mr. McDonagh that his so-called phases of the "leucocytozoon" of syphilis consists mainly of lipoid-globulin "molecules"? How has he demonstrated these "molecules," even in the definitely established spirochæte, and still more so in the highly problematic "spore stages" of the leucocytozoon? I would draw attention to the fact that the lipoids only form loose combinations with proteins, and therefore only loose chemical compounds and not molecules result from their combination. On what evidence does Mr. McDonagh conclude that the lipoid-globulin molecules in syphilitic infection are larger, more numerous, and have a greater adsorptive capacity than normal "lipoid-globulin molecules"? There is no evidence that lipoids play any essential part in the production of antibodies. Specificity cannot be explained by homologous stereochemical molecular configuration of the lipoid-globulins, for, experimentally, an antigen may be completely deprived of its lipoid constituents and the resulting antibody production be in every way the same as if the native antigen has been used, and, *vice versâ*, an antibody, by careful treatment, can be deprived of its lipoids without its properties being affected by such treatment. Mr. McDonagh also states that the reducing action of the spirochætal lipoid-globulin is greater than that of the lipoid-globulin of the host, owing to the presence in the former of non-completely saturated fatty acid. How has he arrived at this conclusion, and has he compared the saturation of the fatty acids of the lipoids of the spirochæte with those of the host, which are known to have a high iodine number?

Mr. JOHN WARD: A very great point in favour of Mr. McDonagh's synthetic compounds is his selection of those containing iron and sulphur. In 1911 the late Mr. Henry Crookes exhibited a number of photographs before the Royal Society showing the action of various metals and non-metals on bacteria. By these photographs it was shown that arsenic was the most powerful bactericide of all the elements, with the possible exception of antimony. It follows that arsenic is also the most powerfully organotropic of the elements. With regard to the action of salvarsan, galyl, intramine, etc., whether the parasites are killed by adsorption of the particular compound or not, it is certain that the element employed is eventually deposited in the tissues, probably in the colloidal condition. Ullmann showed by X-rays that after the injection of salvarsan intramuscularly arsenic persisted in the tissues from a few weeks to many months, and even when injected intravenously it took a long time to eliminate. Is it not probable that the increase in cases of degenerative encephalitis and myelitis may be due to the catalytic action of arsenic in the nerve tissue? It will be seen from the photograph shown that iron is practically non-bactericidal, and therefore probably non-organotropic. Sulphur, far from being bactericidal, exerts a stimulating influence, and therefore may reasonably exert a stimulating influence on the organic cells and tissues. Indeed, it is well known that the arteries and veins contain nearly 1 per cent. of sulphur. With regard to the point raised of oxygen being necessary for adsorption, it is certain that the cells must be in a healthy condition for this to take place, and for this oxygen is, of course, necessary. Comparison should not be made with a rigid structure like charcoal, the specific surface of which cannot vary. Mr. McDonagh's theory of oxidation and reduction seems to offer an explanation of many phenomena which have hitherto seemed enigmas. It is quite reasonable to suppose that the chemical bodies contained in the body of the spirochæte vary in constitution—compare the constitution and amount of alkaloid contained in plants at various times of the year—and it is very highly probable that a different chemical reaction should be necessary for their death. The ultimate end of either a reducing or oxidising agent is, of course, oxygen, and before closing I should like to mention the effect of colloidal iodine in recovery from alcoholism. The alcohol probably forms a film over the cell tissues, causing considerable atrophy with consequent depression. The iodine combines with the alcohol to form ethyl iodide and oxygen, thus restoring the cell to its normal condition. The action of iodine in rheumatism is probably similarly explained.

Mr. McDONAGH (in reply): None of the views expressed either disproves my theories or upholds those of Ehrlich. I am surprised that, in view of the scientific knowledge possessed by the various speakers, so much of it has been used for destructive criticism and none for constructive purposes, and it is particularly to be observed that any reference to the questions asked at the beginning of the paper has been avoided—proof that the general opinion of Ehrlich's theories is that they are illogical. It is impossible to supply in a few minutes the various proofs asked for, especially by Prof. Bayliss, as doing so would entail a recapitulation of the research work done during the last four years. Moreover, many of the doubts raised would not have found expression had the research work referred to been studied. The main object of the paper has been to show that arsenic, a toxic metal, is not essential, and that its place can be taken by iron and sulphur. Ferrivine and intramine were not discovered empirically, but as the result of an ordered sequence of experiments which showed not only that the action of iron and sulphur is mutually complementary, but also that their introduction into the body simulates and accelerates processes which are normally taking place. The clinical cases reported show that the drugs mentioned possess a powerful therapeutic action, but that, being new, there attach to them disadvantages which, in time, can be easily overcome. It is doubtful whether those who decry the value of intramine owing to the pain it causes are familiar with its use. Even in the worst cases the pain cannot be compared with that produced by salvarsan when it first came in. I have administered over 200 injections of intramine without any ill effects, and have obtained results which, in my opinion, prove that it should be used in every case of syphilis.

ADJOURNED DISCUSSION ON THE RATIONALE AND PRACTICE OF CHEMOTHERAPY.

(*Supplementary Paper.*)

By J. E. R. McDONAGH, F.R.C.S.

The main object of my last paper was to point out that once the rationale of chemotherapy was put upon a logical basis, empiricism would vanish and the paths would be open for the preparation of non-toxic drugs. My theory of oxidation and reduction satisfactorily explains the *modus operandi* of chemotherapy. As iron and sulphur are the two elements which play an important *rôle* in these two processes in the body, it stands to reason that suitable compounds thereof will be non-toxic; also that if such compounds are able to exert a therapeutic action in syphilis, it will prove the correctness of the theory, since neither of these elements has a marked parasiticidal action—indeed, sulphur even stimulates the growth of bacteria. Iron and sulphur, in their respective compounds ferrivine and intramine, do exert, if properly employed, a therapeutic action not only in syphilis, but also in many other diseases, which is corroborative evidence of the soundness of the views enunciated. This piece of work is only one link in my chain of research on syphilis, and is based, like the other links, upon the proofs brought forward to show that the *Spirochæta pallida* is not the only cause of syphilis. Until those who are equally interested in the subject of syphilis with myself have either proved my work on the life-cycle of the *Leucocytozoon syphilidis* to be correct or incorrect, they will be unable to appreciate my motive for introducing the drugs, the therapeutic action of which this paper is designed to describe. Intramine and ferrivine have been introduced, first, to form a link in the chain referred to, and secondly to show that a toxic metal like arsenic is not an essential ingredient of the chemotherapeutic preparations. As to whether intramine and ferrivine, as they become improved, are destined to replace salvarsan and its substitutes in the treatment of syphilis, only the future will show.

So far as other diseases are concerned, I can say that ferrivine in the acute stages and intramine in the chronic stages have a more powerful action than salvarsan. Intravenous injections of ferrivine act beneficially in cases of acute ulceration—ulcus molle, for instance. Intramine has a therapeutic action in cases of chronic ulceration, tuberculosis, gonorrhœa, meningococcic infections, etc. The local application of intramine to chronic wounds, sinuses, etc., will bring about in some cases an improvement unobtainable with any other drug. Furthermore, intramine can be taken internally, but with what effect has yet to be determined.

All elements which are parasitotropic are in the same degree organotropic; hence the use of arsenic, antimony and silver will always be fraught with a certain amount of danger. Iron and sulphur are not parasitotropic, therefore they are not organotropic; hence their use can never do the host any harm. As both sulphur and iron stimulate processes that are naturally occurring in the body—processes which are employed to combat all diseases—and as one is complementary to the other, it behoves us to perfect the compounds which contain these elements. The best sulphur compound so far prepared is intramine, and the best iron compound is ferrivine. Intramine has the misfortune to be painful, a disadvantage which with co-operation we should soon be able to overcome.* By its upsetting the hydrogen ion concentration of the serum, ferrivine did at first produce shock, a disadvantage I have now completely overcome. It is also clear to me how its action could be materially increased, but here again co-operation is needed to achieve this result.

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* The disadvantage has now been quite overcome.

The pain produced by intramine varies in different individuals, and in my own cases it never remains severe for more than three days. Provided there is no urea and quinine hydrochloride present, an abscess never forms, and no sloughing nor induration ensues. I have given 287 injections of intramine without experiencing, with the exception of two cases in which a sterile abscess occurred, any ill-effects other than pain. In the two cases referred to, some urea and quinine hydrochloride had been added to the drug. The use of intramine being, as it is, complementary to all the metallic compounds now employed, is in my opinion indicated in every case of syphilis. Its effect in removing the induration of chancres, the resistant papules and the fibrous tissue in the recurrent and late lesions, far surpasses that produced by salvarsan. In syphilis of the nervous system the administration of intramine has wrought results which I have never experienced with other remedies. Furthermore, intramine increases the action of the drugs which succeed it. I had a case of congenital interstitial keratitis which responded to neither mercury nor intramine, but when mercury was prescribed after the intramine had been given, the condition immediately began to mend. I particularly mention this case because it shows so well the action one drug has in helping another, and because cases may be met with which do not respond to the treatment which usually benefits them. One of the tongue cases exhibited to-day also shows this so well—a case of gummatous glossitis which, obdurate to salvarsan, healed up immediately with intramine.

In the primary and the generalisation stages of syphilis, an adsorbed metallic compound must be prescribed before intramine, or the contrary action to that desired may be experienced if the non-metallic compound precedes the metallic. In the recurrent and late stages of syphilis the best results are obtained if intramine be given before an adsorbed metallic compound. Intramine not only increases the action of ferrivine, but also that of the arsenical compounds. Salvarsan and its substitutes have little effect upon the induration of chancres, and some of the cutaneous papular lesions are extremely resistant to these drugs; if in such cases intramine is prescribed after two injections of the metallic compound have been administered, the hardest induration and the most resistant papule will have vanished within ten days.

Ferrivine, as it is now prepared, has no disadvantages; there is practically no limit to the dose that may be employed, and the injections can be repeated as often as is desired—even daily. In some cases of early syphilis its action is quicker and more pronounced than that of salvarsan, while in others it is not so good, for very obvious reasons. The changes produced in the lesions by ferrivine are different from those which follow salvarsan.

Under salvarsan a chancre becomes drier, the surface heals, but the induration takes some time to disappear: the dorsal lymphangitis likewise vanishes slowly, and the hardness in the lymphatic glands persists, often many months.

Under ferrivine the chancre swells, the surface becomes much moister, and does not heal very quickly, but when reparation sets in and the swelling has vanished it will be found that every trace of induration has gone, and no scar is left to mark the position of the sore. The dorsal lymphangitis quickly disappears, and the hardness of the inguinal lymphatic glands gives place to their normal consistency. These changes are increased and accelerated by the addition of intramine. The ordinary early syphilitic rash does not disappear so quickly with ferrivine as it does with salvarsan, the infiltration rapidly subsides, but an erythema marks the site of the macules and papules for some time. The same may be said of the mucous papules in the throat. After ferrivine reactionary inflammation in the lesions is more frequently met with than when salvarsan is the drug used.

Why the changes above mentioned should be so different I cannot at present say, as I have not examined the lesions after ferrivine to see if those phases of the *Leucocytozoon syphilidis* which are not killed quickly by salvarsan are killed by ferrivine, and *vice versâ*. It is possible that the spore stage, which is so resistant to arsenic, may be susceptible to iron, and the opposite the case with the adult sexual phases. That some explanation of this sort is highly probable is suggested by the fact that ferrivine does clinically just what salvarsan does not do, and *vice versâ*. All that can be said at present is that the *Spirochæta pallida* is not killed quickly by ferrivine as it is by salvarsan, a fact which proves nothing, since the adult male phase is not the phase that is responsible for the spread of the disease.

I have given up to date 126 intravenous injections of ferrivine, and have never experienced any toxic symptoms other than shock, which is now avoidable. For the preparation of serum for intraspinal injections, ferrivine and intramine are extremely suitable, and there is no fear of encountering those toxic symptoms which are so liable to follow the use of the substitution products for salvarsan.

No one realises more than I do that intramine and ferrivine are by no means perfect; of their therapeutic action I am fully convinced, and in view of the non-toxicity of the elements iron and sulphur, I feel confident that in time they will replace toxic elements like arsenic, antimony, and silver. As matters stand at present, intramine is called for in every case of syphilis, and the benefit wrought by its inclusion among the antisyphilitic remedies far outweighs the temporary inconvenience caused by the pain. I for one would never hesitate to have intramine if I were so unfortunate as to contract syphilis. I have administered intramine to several medical men, and they have been struck by the rapidity with which the induration of the primary lesions and the late lesions have disappeared. I have also received several reports from medical men as to the efficacy of intramine in cases which did not respond to salvarsan. In view of the different effects produced upon the lesions by ferrivine and salvarsan, it is possible that the employment of both at the same time is indicated. Cases which have not responded well to ferrivine have certainly cleared up more rapidly with salvarsan afterwards than they would have done if the latter had been the only drug employed. It is this fact which makes me think that certain phases are killed more quickly by one drug than the other, and *vice versâ*. My own opinion is that Ehrlich was trying hard just before he died to replace the arsenic in his compounds by other and non-toxic metals, since there have been many more cases of arsenical poisoning than have ever got into print. The following are the cases which I have either seen myself or about which I have had letters since the war started, therefore they are cases which have developed toxic symptoms after the employment of the various substitutes for salvarsan: 3 cases of sudden death; 12 cases of generalised arsenical dermatitis, 2 of which died; 9 cases of mild or localised arsenical dermatitis; a fatal case of cerebral degeneration after an intraspinal injection of serum drawn off after galyl; 3 cases in which the symptoms of degenerative myelitis were very much aggravated, and the degeneration increased by the use of serum injected intraspinally after the administration of kharsivan and galyl; 5 cases of very severe neurasthenia; 4 cases of arsenical neuritis; 6 cases of jaundice; an uncertain number of cases of shock. The symptoms varied from loss of pulse to difficulty in breathing, with asphyxia and swelling of the lips and tongue.

I will now turn to the cases exhibited, which you have all had the opportunity of seeing:

Case 1.—J. C—. Ulcus molle on penis with twenty-seven small ulcera mollia in right inguino-scrotal region. The sore on the penis was deeply ulcerated and about the size of a shilling. Before treatment was commenced the patient had had the sore for six weeks. May 20th, 1916: Intravenous injection of ferrivine (100 c.c.). May 22nd: Most of the small ulcers had healed. May 23rd: Intravenous injection of ferrivine (100 c.c.). June 1: All the small ulcers had healed and the large one was very much better.

Case 2.—P. B—. Syphilis four years ago, for which patient was treated irregularly. Advice was sought for a recurrent serpiginous syphilide of the scrotum. Within a few days after an intramuscular injection of intramine (1 grm.) the lesion completely disappeared.

Case 3.—J. B—. Patient, on examination, was found to have a typical hard, papulo-erosive chancre on the left side of the corona, indurative lymphangitis on the dorsum of the penis, and indurative lymphadenitis. April 1st, 1916: Intravenous injection of ferrivine (300 c.c.). As a result of the injection the sore swelled and became very inflamed. As the swelling disappeared it could be noticed that the induration was much less. The reactionary inflammation was equally marked in the lymphatic cord and glands. April 8: Intramuscular injection of intramine (1 grm.). April 29th: Sore had completely vanished, leaving no scar or induration. The lymphangitis had entirely disappeared, and the lymphatic glands had returned to their normal state.

Case 4.—W. A—. Patient had a well-marked intra-urethral sore, general indurative lymphangitis and lymphadenitis, and a maculo-papular rash. March 18th, 1916: Intravenous injection of ferrivine (300 c.c.). April 15th: Intramuscular injection of intramine (1 grm.) April 29th: The sore had completely vanished, leaving no induration or narrowing of urethra behind. The rash had disappeared and the patient felt extremely well.

Case 5.—H. S—. On examination patient was discovered to have a hard, papulo-erosive chancre on the left side of the corona, a diffuse papular syphilitic eruption of the penis and scrotum, indurative lymphadenitis and gonorrhœa. The foreskin could not be retracted. May 2nd, 1916: Intravenous injection of ferrivine (100 c.c.). Swelling of foreskin disappeared forty-eight hours later. May 9th: Intravenous injection of ferrivine (100 c.c.). Foreskin could be retracted. May 13th: Intramuscular injection of intramine (1 grm.) Induration completely disappeared, sore healed, and the other symptoms vanished except the gonorrhœa, which had only slightly improved.

Case 6.—T. W—. When seen patient had a swelling of the penis which, from the feel, allowed the diagnosis of a hidden primary sore to be made. Foreskin could not be retracted. There were the usual lymphangitis and lymphadenitis. May 16th, 1916: Intravenous injection of ferrivine (100 c.c.). Forty-eight hours later swelling had disappeared. May 20th: Intravenous injection of ferrivine (100 c.c.). Forty-eight hours later foreskin could be retracted. May 23rd: Intravenous injection of ferrivine (100 c.c.). When examined three days later, it was seen that there had been a gangrenous chancre of the glans penis. The ulceration had practically cleared up, and the lymphangitis and lymphadenitis had vanished.

Case 7.—G. P . Patient presented himself with a huge swollen and indurated penis. There was a large chancre on one side of the prepuce and another on the other side, as well as an ulcerative chancre of the glans penis. Lymphangitis and lymphadenitis were present, there was a diffuse maculopapular rash, and mucous papules in the mouth and around the anus. March 28th, 1916: Intravenous injection of ferrivine (300 c.c.). Seven days later the two preputial sores had healed, the lymphangitis and lymphadenitis had disappeared, and the rash was very much fainter, but the mucous papules remained about the same. April 15th: Intramuscular injection of intramine (1 grm.). May 6th: Intravenous injection of ferrivine (100 c.c.). As the result of the last two injections the chancre on the glans penis entirely disappeared, but one or two of the mucous papules remained.

Case 8.—J. J—. Syphilis seven years ago, for which patient was irregularly and inadequately treated. About a year ago the tongue became swollen, painful, and ulcerative, and its movements were restricted. April 29th, 1916: Intramuscular injection of intramine (1 grm.). Some days later the tongue, with the exception of some patches of leucoplakia, returned to its normal condition. The improvement commenced forty-eight hours after the injection.

These cases, I think, show conclusively that intramine and ferrivine have an antisyphilitic action. This being the case, and since it is obvious to me how the therapeutic action of these drugs could be enhanced, and since sulphur and iron will never produce such ill-effects as those I have just related as occurring with arsenic, I feel that not a stone should be left unturned to secure co-operation amongst one another, and to make ourselves pioneers in a field which has not yet been exploited by Germany. When the improvements which suggest themselves have been produced, I feel certain that our treatment of syphilis will be better than it has been with salvarsan, because I am perfectly convinced in my own mind that, however rapidly salvarsan may get rid of symptoms, it most certainly does not cure syphilis.

Discussion.

Dr. J. J. Pringle: My remarks will be directed almost exclusively towards the clinical aspects of Mr. McDonagh's paper. In order to qualify myself for making these remarks with any degree of pertinence, propriety, or assurance, I have for many weeks past pursued the perfectly obvious course of attending

Mr. McDonagh's clinic at the Lock Hospital, where every facility has been afforded me of observing and following out his cases as far as that is possible in out-patient practice. According to my knowledge it is only at the Lock Hospital, apart from military hospitals, that sufficiently abundant material can be found, even in London, for drawing conclusions of decisive value as regards the efficacy of treatment of the primary lesion of syphilis. And surely the success, or otherwise, of treatment of the initial chancre is the best criterion at our disposal for estimating the value of any remedial measure? In other words, the cutting short of syphilitic disease before its systemic generalisation is, whenever attainable, the main and paramount object of our therapeutic attack. The value of salvarsan and other bodies of the arseno-benzol series in aborting the primary chancre is manifest and indubitable; but I say without hesitation that the results obtained in similar circumstances by ferrivine—as I have witnessed them—are even more striking and immediate. The local reaction is, generally speaking, less severe, and, although the shock and collapse which follow an overdose are certainly sometimes alarming, they are almost always of short duration. The general reaction which ensues upon the injection of 1 grm. in 100 c.c. of sterilised distilled water (the dose now established as the normal), if present, is quite negligible. The injection may with safety and advantage be repeated on two or three occasions, at intervals of only a few days, owing to the non-toxicity of the drug. I may sum up my views on this all-important branch of the subject by saying that the results of treatment by ferrivine as regards the complete and rapid healing of the primary sore, with subsidence of its induration, must be seen to be believed. Coming well within the sphere of influence of ferrivine are the implication of the lymphatics of the penis and of the immediately adjacent lymphatic inguinal glands. These yield in a manner which I believe to be unprecedented. When an early roseolous eruption is present, a well-marked local aggravation, apparently on all fours with the Herxheimer reaction, may occur immediately after or even towards the end of the injection of ferrivine; this indicates, I cannot but think, that the *modus operandi* of ferrivine is essentially parallel to, or identical with, that of arsenical preparations. I have not seen aluvine used.

The clinical evidence of the therapeutic value of intramine appears to me much less positive, less tangible, less capable of definite appreciation, more elusive, and it is in the nature of things that it should be so. My opportunities for estimating its value have not been confined to what I have seen at the Lock Hospital, as in the case of ferrivine, but have been derived also, and chiefly, from the study of its employment in a number of cases of so-called secondary and tertiary syphilis in my own hospital practice, where good opportunities are afforded for close and continuous observation. My experience leads me to endorse, on the whole, Mr. McDonagh's view that intramine is a most valuable adjunct, or rather adjuvant, to treatment by arsenical or iron salts in cases of early cutaneous syphilis. I customarily use galyl as my principal instrument of attack in such cases, and I have convinced myself that the additional employment of intramine has accelerated the disappearance of hard papular or nodular syphilides, as well as those of follicular, racemose, and corymbose type (which are notoriously and universally acknowledged to be obstinately resistant to ordinary methods of treatment), and in one case of a deeply pigmented rash its use was followed by a remarkable and unexpected recovery. A word of caution may, perhaps, be pronounced against the risk of administering intramine at too short a period after an arsenical preparation, On one occasion, in which I was constrained by circumstances to give an injection of intramine to a woman who had had 0·4 grm. of galyl less than twenty-four hours previously, the characteristic symptoms of an acute galyl poisoning (so well known to all who have wide experience of that drug) were faithfully reproduced. I content myself with recording the fact as a warning, without entering into any attempt to explain the rationale of its occurence. There can also be no doubt in my mind of the value of intramine in late superficial recurrent cutaneous syphilides, one injection often sufficing to cause their rapid disappearance, and this observation of Mr. McDonagh's is fully borne out by several cases in my own practice. I speak with less confidence as to the efficacy of intramine employed alone in late gummatous manifestations. The cases of this type in which I have been able to witness its efficacy have all been treated either previously or synchronously with arsenical preparations, the relative value of which it seems to me impossible to estimate or discount. I have personally seen nothing of the results obtained by ferrivine or intramine, either in combination or employed alone, in cerebral or spinal meningitis or in degenerate encephalitis or myelitis; but I may, perhaps, state in passing that I agree to the full with Mr. McDonagh, that all of these complications have been of much more frequent occurrence since the introduction of salvarsan and other arsenical preparations. I have also no experience to record as to the value of these two drugs in interstitial keratitis or other manifestations of congenital syphilis.

It would be a poor compliment to him, and my contribution to this debate of very dubious utility, if I did not submit Mr. McDonagh's originally conceived and almost revolutionary work to some unbiassed criticism. My first and most obvious observation of this nature is that the time is far too short and the amount of observation yet far too small to admit of any definite conclusions being drawn as to the permanence of the results obtained. We must all remember the numerous and sad disillusioments which too frequently followed the bright early promise of salvarsan. It appears to me, however, that the undoubted superiority of action of ferrivine, which I believe to have witnessed, and probably of other corresponding metallic salts in the primary lesions of syphilis over arsenical preparations, gives some *prima facie* probability of their ultimate action being also more complete and more permanent. All the cases of primary syphilis I have seen treated with ferrivine have been in men, and I question gravely in what proportion of women (with abundant subcutaneous fat and small flaccid veins) such bulky intravenous injections would be tolerated. The great pain resulting from the intramuscular injection of intramine has been loudly proclaimed—almost acclaimed—from many sides. The cry is, I think, to some extent justified. In my own experience the pain, which does not immediately succeed the injection, and which is accompanied by rather high temparature, renders the patient unfit for work for more than a week. In only two instances have I been able to persuade a patient to have two injections of intramine, and both were stalwart men particularly keen to be passed into the Service. This is a widely different experience from that of Mr. McDonagh, who goes so far as to recommend "eight fortnightly intramuscular injections of intramine" alternating with mercurial intramuscular injections. I can scarcely conceive of intramine being applicable for congenital syphilis, but I am bound to add that I have seen cases in which it apparently caused no pain nor pyrexia. And I am aware that the preparation of an intramine derivation is already on the way, if not actually on the market, which is less painful.

I have observed with a feeling almost akin to sadness that Mr. McDonagh has thrown overboard our old friend the Wassermann reaction. I am well aware that the Wassermann reaction is an excellent servant and a bad master. I realise fully that complete reliance upon it to the exclusion of other clinical methods of observation has led to much bad practice on the part of the medical man, and to much disappointment and even suicidal syphilophobia on the part of the patient. But I am still of opinion that the Wassermann réaction, intelligently employed, is a valuable aid to diagnosis in many cases where diagnosis is doubtful, and is a precious indication of the success or non-success of treatment in carefully appreciated cases. I admit that I do not understand the nature of the substitute for the Wassermann reaction which Mr. McDonagh proposes.

I pass over, for the sake of time, many points which might perhaps be raised and discussed with advantage. There is no doubt that to the medical "man in the street" the opinion is still prevalent that the object to be held in view in the treatment of syphilis is a destructive frontal attack of the element arsenic upon the spirochæte. This theory has, I venture to think, received its death-blow from the researches of Mr. McDonagh and the success of his treatment founded upon them. We, as dermatologists, probably appreciate more fully than the majority of syphilographers how grave the results of the prolonged administration of arsenic may be; and there cannot, I believe, be any doubt that the employment and substitution of the remedies, which are in the ordinary sense of the word non-toxic, constitute an immense advance upon our procedure up to date.

May I be permitted, as a past President of the Section, to offer to Mr. McDonagh my congratulations upon his work, which has been carried out in troublous times, and, to my knowledge, in circumstances of great difficulty—work which is eminently original in conception, and which opens up a great and fruitful vista of therapeutic utility? And may I likewise congratulate the Section upon the honour of having had this admirable piece of all-British work brought forward and discussed at its meetings?

Lieutenant-Colonel L. W. HARRISON, R.A.M.C.: At the last meeting very little was said on the biological side of the question. Possibly because those who had any views on the matter felt that if they did not agree with Mr. McDonagh's microscopical interpretations it would be a waste of your time to discuss here matters which could only be settled with the help of a battery of microscopes and an interminable argument. Still, it may not be out of place to discuss the matter on general lines. Mr. McDonagh published his first description of the life-cycle of the micro-organism of syphilis, unless I am mistaken, in 1912. It appeared in English and German periodicals, and Mr. McDonagh read a paper on the subject at the last International Congress, so that I think we can safely say that it has been widely read. He has shown his specimens here and at other societies, including the Pathological Society of Great Britain, so that many expert microscopists have seen them. Further, it is probably true that most biologists who are interested in the subject are favourable to the idea of the micro-organism of syphilis having a life-cycle. It is an idea which has been in vogue almost since the *Spirochæta pallida* was discovered, and it is quite certain that biologists all the world over would be eager to take up any work on the subject. Yet, does it not seem strange that not a single word of confirmation of Mr. McDonagh's interpretations has appeared in print from any microscopist of standing? Actually, to-day, the *Leucocytozoon syphilidis* has not a single friend outside its birthplace. Is this the fate of sound discoveries in these days? Are we to assume that those who confirmed in less than three months the discovery of the *Spirochæta pallida*, the Wassermann test, and Noguchi's discovery of spirochætes in the brains of general paralytics—that is to say, biologists all over the world—are so unworthy as to withhold confirmation of this one of Mr. McDonagh's on personal grounds? As I have said, the biological world is ready for, and would welcome, the discovery of a life-cycle of the micro-organism of syphilis. But it does not accept the *Lucocytozoon syphilidis*. Mr. McDonagh has built up on this biological foundation a chemistry of syphilis which is so intricate and its terminology so strange in many respects that, as you heard at the last meeting, expert chemists cannot understand it. We may leave it at that. However, let us grant for a moment that the other biologists and chemists are all wrong; or, if you like, that even if Mr. McDonagh is wrong, he may still have produced remedies for syphilis which are an advance on present treatments. If he had we would gladly leave the chemists and biologists to their quarrel and accept the remedies. Which brings me to the clinical side of the question. Are ferrivine and intramine specific remedies for syphilis? The firm which is responsible for the manufacture of these compounds very kindly gave me some samples of them, and nothing would please me more than to be able to say they are all they claimed to be. For the test we took at first three untreated cases of ordinary secondary syphilis. They were cases with lesions from which it was easy to obtain the *Spirochæta pallida* and which we could watch easily from the point of view of clinical progress. Two of them were injected with two doses of ferrivine, then a dose of intramine, and lastly a dose of ferrivine. One received two injections of ferrivine only. All of them were examined daily for spirochætes and for changes in clinical lesions. I should like to say here that the cases were under the immediate care of Mr. Mills, whose detailed notes would, I am sure, interest you. I can confirm them from my own daily observation of the cases and agree entirely with Mr. Mill's descriptions. I will leave the details to him and confine myself to a summary of the results of our observations.

First, as to the reactions which ferrivine and intramine cause. The reaction from ferrivine is distinctly alarming. Briefly, it amounts to acute respiratory distress, signs of collapse, epigastric pain, and most severe vomiting. The temperature may rise to 103° F., or higher, and the patient is acutely ill for some hours after the injection. The injection of intramine is followed by a local reaction, which is, if anything, worse than that which follows the intramuscular injection of salvarsan. Judging by the patient's description of it one would say it was undiluted torture. I should mention here that four other cases had been treated with intramine some weeks before we started this series, and we have since injected another case, so our experience of the local reaction caused by intramine is based on eight cases. It was practically the same in all of them. The local swelling and tenderness last for weeks, and abscesses have been opened in two of our cases. One of these is still discharging after twelve weeks, and will take many more weeks to heal up. In those cases where no abscess has yet burst outwardly it is easy to feel by the gap in the muscles that there has been considerable necrosis there. Altogether, we have good grounds for disagreeing with Mr. McDonagh when he says that intramine does no permanent damage. I cannot accept, either, any imputation as to the technique of these injections. They were most carefully carried out, with the strictest attention to aseptic details, and the greatest care was taken to make them strictly intramuscular. Nor were quinine and urea used. I lay stress on the reactions which follow intramine and ferrivine because they are severe enough in themselves to make these compounds quite impracticable for general use, even if they had any therapeutic value. As to the therapeutical effects of intramine and ferrivine, I will omit the four cases which we treated earlier with intramine because they are not a fair test. They were all secondary cases, and the fact that intramine had no effect on their lesions proves nothing against it. Mr. McDonagh had said that ferrivine is like salvarsan—a metallic compound which acts only on the *Spirochæta pallida* and the impregnated female. We may consider whether ferrivine acts on the *Spirochæta pallida*. It certainly did not do so in our cases. *Spirochæta pallida* was found just as abundantly for ten days or longer after the first injection of ferrivine as on the day before it was first given. After one case had been injected with two doses of ferrivine, one of intramine, and then another of ferrivine, a mucous patch made its first appearance on one tonsil, and *Spirochæta pallida* was found in the new lesion. Another case was very instructive. He received two injections of ferrivine, but a mucous patch inside the upper lip remained absolutely unchanged, and *Spirochæta pallida* was recovered from it for a week—in fact, right up to the day on which we at last gave the patient an injection of 0·3 grm. salvarsan. On the morning after the salvarsan injection we were unable for the first time to discover spirochætes in the patch, and on the next day the lesion had healed: surely a striking example of the comparative merits of salvarsan and ferrivine, which Mr. McDonagh has told us are alike in their therapeutic effects? As I have said, the addition of intramine to the treatment of the cases failed to produce any better effect. We have since treated with intramine a case of multiple skin gummata in all stages of development; such a case, as we know, does particularly well on salvarsan treatment. The only effect of the intramine has been to give him a buttock which at one time was three times the size of its fellow. So far from any beneficial effect having followed the injection, at least one of the gummata broke down, and all the lesions behaved as if no treatment whatever had been applied. Yesterday I reluctantly consented to this patient receiving an injection of ferrivine. I witnessed the injection and the reaction which resulted from it. In the course of a few minutes I saw a ruddy, healthy-looking man rendered pulseless, gasping for breath, restless, and as nearly dead as I ever want to see any patient. I shall not forget the scene, and if I can ever save a patient from being injected with this remedy I will do it.

On a biological foundation, which has not been confirmed by anyone of standing, and a chemistry which nobody seems to understand, Mr. McDonagh has invited—I might almost say commanded—us to forsake salvarsan for ferrivine and intramine. We have found his substitutes not only extremely unpleasant in their effects, to put it mildly, but they have failed to affect three perfectly straightforward cases of early syphilis and one of tertiary—three of them cases which we know would have healed in a week or ten days under salvarsan. Would anyone consider me justified in subjecting any more patients to the injection of these compounds? For myself, I am satisfied, and shall be content to let somebody else's patients bear the brunt of any further experiments with them. I must admit that I had very great compunction about submitting our patients to the intramine torture after ferrivine had failed so miserably to affect their lesions. I have doubts now as to whether I was justified in giving these injections, but if our experience serves to save any further victims, then our patients have not suffered in vain. As to Mr. McDonagh's cases, they carry no conviction to my mind. He says nothing of any standard laboratory test which supports his diagnosis, and in an inquiry of this kind it is unwise to trust any diagnosis which is not supported in this way. As to the effect of a remedy on tertiary lesions, even a good effect does not prove the remedy to be specific for syphilis. Everyone has seen tertiary lesions disappear under the most various non-specific treatments. I lately saw a woman who for years had successfully treated her recurring gummata with the application of nothing more specific than hot water.

I am afraid I have been rather severe in my criticism. I have favoured a German compound at the expense of a British. I would ask you to believe me when I say it is not because the one is German and the other British, but because it is vital that we should choose the right remedy, whatever the country of its origin. Mr. McDonagh has exhorted us not to imitate German methods but to support British science and discovery. I echo the sentiment. But is the method which he has adopted of introducing intramine and ferrivine likely to enhance the reputation of British science? I can find no parallel for its dogmatism and other features except in German literature, and if there is one thing more than another which has bred in me a healthy scepticism of remedies which are introduced with a flourish of trumpets it is my experience of the many useless German compounds which I have tested after reading the perfectly convincing articles of their German authors. Ferrivine and intramine have been introduced to the medical public on the strength of a few trifling preliminary experiments. In contrast to salvarsan, which was not placed on the market until 20,000 doses of it had been tried in accredited clinics, these new compounds have been thrust upon private practitioners before any report on them has been received from any independent clinic. I feel very strongly that the course pursued by Mr. McDonagh in introducing these remedies is likely to result sooner or later in a disaster which will not only be terrible in itself, but will have a bad effect on the progress of therapy.

Dr. J. H. SEQUEIRA: In the first place, Sir, I beg to tender to Mr. McDonagh my congratulations on the interest which his work has aroused. I regret that I could not be present at the first meeting, but as the Editorial Representative of the Section I have had the privilege of carefully reading both the opening paper and the discussion. I feel we owe some recognition to the distinguished biochemists who, at the invitation of the officers of the Section, came to give us the benefit of their criticism on this intricate subject. We must also regret that time prevented Mr. McDonagh from answering in detail some of the important points raised by Prof. Bayliss and others. A survey of the paper shows that it is divisible into two parts: one which is highly speculative and theoretical, and the second which offers us new drugs—"intramine," which is said to have an almost universal application, for it is claimed to be of value not only in syphilis but also in tuberculosis, lepra, and even in old shrapnel wounds; and "ferrivine," which is specially useful in the treatment of syphilis. On the theoretical side I confess my inability to follow much that has been put forward, and after a careful search in the writings of Mr. McDonagh I have failed to find detailed accounts of the experimental work upon which it is based. I may, however, be permitted to refer to two points: Mr. McDonagh admits that we have no knowledge of the chemical composition of the lipoid-globulin bodies of which the parasite of syphilis is said to be composed, yet we learn that the "adult male spirochæte and the impregnated female spirochæte are affected by certain remedies in virtue of their free hydroxyl groups." The virgin female spirochæte and the spores lack these free hydroxyl groups, and are therefore unaffected. What proof is offered in favour of this remarkable statement? In passing, I should like to thank Mr. McDonagh for using the word "spore" in this paper. It was so troublesome to be obliged to have a Liddell and Scott by one, and the simpler term suggests a change towards the views of Balfour, Leishman, Noguchi, Fantham, and others. My second question on this side is suggested by the statement that certain lipoid-globulin molecules increase in size during the evolution of syphilis and also in response to certain drugs. Upon this growth of molecules some important deductions are made. In all humility I ask, How does one recognise the growth of a molecule? To come now to the practical points: We are asked to discard the remedies whose inception we owe to Ehrlich and Hata, remedies which, we may remember, were given a prolonged trial in a number of clinics before they were put on the market. I think I am correct in stating that the author of the paper was one of the gentlemen in this country to whom Ehrlich sent material for experiment. We have now had some years' experience of the salvarsan group of drugs, and before we discard them let us ask ourselves for what reasons a drug or drugs should be discarded. In my opinion there are four reasons: (1) If one can replace the remedy by one of greater therapeutic value; (2) if a drug causes toxic symptoms and can be replaced by one that is non-toxic; (3) if it can be replaced by a remedy equally efficacious which causes no pain or discomfort; (4) if, while equally efficacious, the substitute is less expensive. Let us examine these points in order.

(1) In my own limited experience of ferrivine and intramine, I have seen nothing approaching the therapeutic results I have been accustomed to see after injecting salvarsan, neo-salvarsan, galyl, and nov-arseno-benzol. Mr. McDonagh himself says: "In *some cases* ferrivine is superior to salvarsan" (the italics are mine). So that I presume it is usually not superior. Further, has this treatment had a year's trial? I think I am right in saying that intramine was put on the market (that is to say, it was available for persons not working at the Lock Hospital) three months ago, and ferrivine came out a month later. I, like Colonel Harrison, have only used these remedies as

they have been supplied to me from the drug house which makes them. Mr. McDonagh states that he is accustomed to pursue a certain course for a year and the course follows a definite ritual for different types of case. Is it not a little early to be dogmatic when the ultimate results are hardly yet observable? We do not yet know the ultimate value of the salvarsan treatment and shall not for some years.

(2) The degree of toxicity of the arsenical compounds is now known. We are informed that ferrivine is absolutely non-toxic, and that doses of 2 grm. and upwards may be given with impunity. I have not given more than 1 grm. for a dose, but I have seen obviously toxic symptoms (and I need hardly insist that a drug may be toxic yet not lethal) in every case. Air-hunger and shock are common, for instance. In a perfectly healthy man with a primary chancre, intense collapse immediately followed the injection. He required energetic stimulation before he recovered. Ferrivine is the most rapidly acting emetic I know; severe vomiting may occur even before the needle is withdrawn. Violent diarrhœa with abdominal pain is also a frequent phenomenon. The effects are almost identical with those which may follow the intravenous injection of an antimony compound, and antimony has a much higher specific gravity than iron. So far I have seen no toxic effects from intramine. There may be a slight degree of pyrexia, doubtless due to trauma.

(3) Intramine, however, causes intense pain and discomfort when injected into the muscles, and my experience entirely confirms that of Colonel Harrison and Captain Mills. Even five and six weeks after an injection massive, tender, painful swellings may be left in the site of the injection, comparable with those seen after the intramuscular injection of salvarsan. I find it almost impossible to get a patient to submit to a second injection, and until I have more evidence of its therapeutic value I am not inclined to urge it.

(4) As to expense, Mr. McDonagh, in a recent article in the *Practitioner*, informed us that there was an enormous difference between the cost of manufacture of the salvarsan compounds and their selling price, but the new remedies, even if they are as efficacious, are little, if any, less expensive.

In conclusion, I am satisfied that, at this present time, there would be no advantage—and, indeed, certain grave disadvantages—in discarding the remedies which have developed from the work of Ehrlich. We know that these remedies have a definite therapeutic value, though they do not fulfil all the hopes which were once entertained. Why should we replace them by drugs which cause serious, if transitory, symptoms, or intense pain and discomfort, without benefiting our patients to an equal extent?

Mr. A. SHILLITOE: I have here the reports of nine cases kept for me by Dr. Bonard, Resident Medical Officer to the Female Lock Hospital. I was particularly interested when first I learned that Mr. McDonagh was working on sulphur. We all know that from quite early times the benefit derived from the use of sulphur-containing waters, in many skin conditions, was considerable, though exactly how the sulphur acted was not generally understood. One hundred years ago it was the custom of certain medical men to treat cases of malignant syphilis or cases cachectic from the abuse of mercury, not with sulphur water but with sulphur-fume baths, and with very great benefit. For some years past it has been my custom in dealing with a severe case of syphilitic cachexia, or a case going rapidly downhill from mercurial poisoning, to use no other treatment at first save sulphur-fume baths, and in a very short time the improvement is so great that ordinary treatment can be employed. I cannot explain how the sulphur acts, I only know it does so most markedly. Of the nine cases, in Cases 1, 4, 5, and 9, the improvement was marked; in Cases 6, 7, and 8 not so pronounced; Case 8 developed a fresh lesion after the conclusion of the course; in Cases 2 and 3 little or no improvement; in Cases 2, 3, 5, 6, and 7, all the lesions became at first more pronounced after the injection of ferrivine; in Case 9 the reaction to ferrivine was much greater than that to intramine. The pain following the injection of intramine was obviously severe in six of the cases; in the remaining three there were no complaints. The pain generally started forty-eight hours after the injection, and lasted for two or three days, and was sufficiently severe to cause the patients not to look forward with any pleasure to the next injection. In none of the cases did an abscess develop. Some of us may remember how very painful were certain of the mercurial injections—*e. g.* sal alembroth, cyanide, and biniodide, used years ago. Calomel was formerly so exquisitely painful that certain French authorities said we were not justified in using it. However, acting on improvements suggested by the late Colonel Lambkin, we used it in the Lock Hospital frequently and painlessly in a very large number of cases. Salvarsan, as originally used, was often most painful, but nevertheless it did not debar us from employing it. I think we may honestly claim that these few cases show that ferrivine and intramine have an antisyphilitic action, in some cases as rapid as those exhibited by salvarsan, in others perhaps not so. As iron and sulphur are less toxic elements than arsenic, it certainly appears to me that a united effort should be made to produce compounds thereof which have an enhanced action over those at present obtainable. The present war has brought home to us all in how many ways we were absolutely dependent on our enemies for necessities in daily use. I do think McDonagh has done or is doing a great work in arousing us from the state of lethargy into which we had sunk. Undoubtedly the one objection to the use of intramine is the pain resulting from the injection thereof. But I think we may look forward with confidence to the time when perhaps, with the aid of friendly suggestions from members of this Section, we will overcome this difficulty.

I must say, apropos of what Colonel Harrison and Dr. Sequeira said, that it was only in two cases out of the nine that we had a really bad reaction from the ferrivine. Certainly in Case 9 the reaction was rather terrifying for the time being. Dr. Bonard informs me that we did have one case of aseptic ulcer, and that was the only one. There were no complications whatever in any of them.

Dr. H. G. **Adamson**: I have not given any injections of intramine in syphilis, only in lupus. I have given sixteen injections of intramine in eight cases of lupus, and at first I thought I was going to get most excellent results. In the first two cases injected there was remarkable improvement, and those were cases in which there were ulceration and crusting. The ulceration healed up at once and the infiltration seemed less. But I am still going on with these experiments, and I cannot usefully say anything further about the matter now. The difficulty consists in getting the patients to submit themselves to further injections, though I think that difficulty is not so serious as some speakers would have us believe. One of my patients has had four injections, and is ready to have another, on account of the improvement which has taken place in the lupus. But I feel it is as yet much too early to say whether it is going to do lasting good in lupus. There can be no doubt that the injection is painful, and it keeps the patient in bed for three days at least, so that it is necessary to take the patient into hospital, and as there are not many beds available it is rather a slow process.

Mr. C. H. MILLS: The following are the clinical notes of the four cases mentioned by Colonel Harrison, and are mostly details as to the microscopical findings in the daily examination of lesions, with observations as to progress.

CASE 1.—R—, aged 27 years. Healed indurated frenal chancre of two months' duration; anal mucous patch (dry); pigmentation of macular rash still present on trunk; mucous patch on upper lip, fauces ulcerated; *Spirochæta pallida* present. May 3rd: First injection of ferrivine, 1 grm., diluted to 200 c.c. with distilled water: vein washed through afterwards with normal saline; patient became extremely collapsed on table with respiratory distress: pain in epigastrium followed by repeated vomiting; vomited during the night in ward, slight rigor; temperature 100° F. May 4th: *Spirochæta pallida* still present in mucous patches; patient recovered from reaction. May 5th: Second injection of ferrivine, 1 grm. (technique as above); patient again collapsed on table and vomited: profuse perspiration; temperature 99·4° F. May 7th: Veins of both arms thrombosed; *Spirochæta pallida* still abundant on unaltered mucous patch on lip. May 9th: *Spirochæta pallida* still present in same. May 10th: *Spirochæta pallida* still abundant in the morning; it was here decided to discontinue the ferrivine course, and 0·3 grm. salvarsan was administered without reaction May 11th: *Spirochæta pallida* disappeared from mucous patch (which has markedly altered in appearance) eighteen hours after 0·3 grm. salvarsan injection. May 12th: Mucous patch healed; no *Spirochæta pallida* found after a thorough search by different observers.

CASE 2.—F—, aged 25 years. May 1st, 1915: Multiple indurated ulcers in coronal sulcus of glans penis; papular lichenoid syphilide, nape of neck, around elbows, and over both hips (symmetrical), also faint erythema; *Spirochæta pallida* present in chancres: no albumin in urine. May 1st: First injection of ferrivine, 1 grm., solution diluted to 200 c.c. with distilled water; vein washed through afterwards with normal saline; severe reaction whilst on table; respiratory distress: pain in epigastrium; pulse very weak, profuse perspiration, vomited; slight rigor, 6 p.m.; temperature 101·2° F. May 2nd to 5th: *Spirochæta pallida* in chancres on daily examination; vein used for injection thrombosed; rash unaltered. May 5th: Second injection of ferrivine, 1 grm. (technique as above); similar reaction and vomiting; temperature 101·6° F. May 7th: 1 grm. intramine injected intramuscularly. May 8th: Bad night; severe pain from intramuscular injection; patient vomited during night; temperature 101·6° F.; *Spirochæta pallida* still present in chancres, which is not yet healed. May 10th: Third injection ferrivine, 1 grm.; less reaction; patient vomited in ward; temperature, 101·6° F. May 12th: Veins of both arms thrombosed; cannot bear pressure at site of injection of intramine; *Spirochæta pallida* still present. May 14th: Fresh papules appeared on both flanks; snail-track ulcers developed over right tonsil; *Spirochæta pallida* present in same; both new lesions; intramine injection very painful and swollen. May 16th: Both fauces ulcerated; *Spirochæta pallida* present; penis healing; intramine injection painful, infiltrated, and fluctuating in centre. May 17th: Treatment with salvarsan and mercury commenced.

CASE 3.—D. M—, aged 38 years. Condition on admission (May 2nd, 1916): Large indurated mass at frænum under phimosed prepuce; duration approximately six weeks; profuse papulo-pustular rash general, general adenitis, anal mucous patch. moist papules on scrotum and inner surface of thighs; fauces ulcerated; no albumin in urine. *Spirochæta pallida* present in moist papules by dark ground examination. May 3rd: 3.30 p.m.—First intravenous injection of ferrivine solution, 1 grm., diluted to 200 c.c. with distilled water, and vein washed through with normal saline; whilst on table patient exhibited sudden respiratory distress, pain in epigastrium; turned ashy-grey colour; pulse became imperceptible; broke out into profuse perspiration and was then violently sick. 6 p.m. —Rigor, temperature 102° F., vomited again, severe headache; diarrhœa ensued during the night, with persistent vomiting; symptoms subsided the following day; temperature 99° F. May 4th: *Spirochæta pallida* still present in moist papules. May 5th: Second injection of ferrivine, 1 grm. (same technique); similiar reaction to above; severe rigor at 6 p.m.; temperature 103·4° F.; *Spirochæta pallida* still present; vein used at previous injection now thrombosed. May 7th: Injection of intramine, 1 grm., into gluteal muscles; "rough night," pain excruciating; *Spirochæta pallida* still present in moist papules. May 8th: Site of intramine injection very swollen and tender; marked œdema of lumbar pad; patient unable to lie on side of injection; *Spirochæta pallida* still present in moist papules. May 9th: *Spirochæta pallida* still present; patient somewhat more comfortable. May 10th: Third injection of ferrivine, 1 grm.; reaction not so severe, but patient again vomited; temperature 99° F. May 12th: Rash beginning to fade (nine days after first injection); papules on scrotum still moist; *Spirochæta pallida* present; site of intramine injection swollen and tender; superficial veins of both arms thrombosed from insertion of deltoid to 6 in. above wrist. May 14th: *Spirochæta pallida* still present. May 16th: *Spirochæta pallida* abundant in chancre. May 17: Site of intramine injections infiltrated and painful; much albumin present in urine, with epithelial casts; ulceration of fauces more marked; treatment with salvarsan and mercury commenced

CASE 4.—P—, aged 39 years. History: Contracted syphilis four years ago. Commenced treatment during the secondary stage consisting of mercury pills and mixture, and continued same for two years; five weeks ago a gumma developed over the head of the left fibula. Condition on admission: He now has multiple gummata on each leg; some can be felt as nodules in the muscles, some subcutaneous, and others in the various stages of necrosis with resultant ulcerations; there is one large ulcer situated over the left popliteal space; the upper extremities, head and trunk are unaffected excepting for one small gumma over left lower ribs; pupils react equally well to light and accommodation; reflexes normal; Wassermann reaction positive. May 24th, 1916: 1 grm. intramine injected into the muscles of left gluteal region. May 25th; Patient passed a sleepless night from exquisite pain at site of injection; hot fomentations applied. May 26th: Left buttock very tender, painful and swollen; morphia administered. May 30th: Much œdema of lumbar cushion; no albumin in urine; pain from injection less; swelling more localised, and can be made to fluctuate. Gentle massage followed by hot fomentations; two gummata, which had not previously involved the skin, have now broken down and are discharging through same. May 31st: Two fresh gummata have developed over the head of the right fibula. June 1st: To this patient I administered yesterday 1 grm. of ferrivine (solution diluted to 200 c.c. with distilled water) intravenously. It was not without a feeling of grave responsibility that Colonel Harrison finally gave his sanction to this injection, taking into consideration the reactions previously witnessed during and after the introduction of ferrivine. I must state emphatically that the reaction which resulted in this instance was the most severe I have ever experienced after an intravenous injection of any of the antisyphilitic remedies with which I have worked up to the present—that is to say, in an experience of upwards of 9000 intravenous injections. The alarming symptoms came on towards the end of the injection, commencing with severe epigastric pains, followed by marked dyspnœa. The pulse then became imperceptible, and the patient turned an ashy-grey colour, when strychnine was immediately administered hypodermically, and for a period of five minutes there was a grave doubt as to the patient's survival. He was finally resuscitated and passed a disturbed night; he was still having rigors when last seen this morning. [June 9th: The above reaction gradually subsided, with occasional attacks of vomiting, by the morning of June 2nd. At the date of this note the gummata have shown no signs whatsoever towards repair. There is a large fluctuating and very tender swelling at the site of the intramine injection.]

Conclusions.—The first three cases above described were chosen simply by virtue of their exhibiting abundant clinical manifestations in order that the therapeutic effect of these drugs could be watched by several observers from day to day. There were present accessible lesions from which the *Spirochæta pallida* could readily be obtained, and so a daily search for the same was rendered both simple and accurate by the dark ground illumination. Now it might be urged, of course, that it is absurd to attempt to form any opinion upon but four cases which have been subjected to this combination of drugs. But I would point out that, having at the present day upwards of five years' clinical experience with salvarsan, we are justified in drawing a comparison, and in stating as a result that one injection of the latter drug would have done more towards clearing up the lesions in these cases in twenty-four hours than did the whole four injections of the drugs under discussion. Again, there is no getting away from the fact that the mucous-membrane lesions—the most infectious, but happily the most amenable to treatment of all lesions—were as rich in *Spirochæta pallida* after the ferrivine injections as before. One knows that one injection of salvarsan, even 0·3 grm., is sufficient to render the finding of the *Spirochæta pallida* in a mucous patch an extremely rare occurrence within but twenty-four hours of the injection. This was emphasised in the case in which two injections of ferrivine failed in any way to affect the mucous patch on the upper lip, either with respect to the healing of the lesion or in bringing about the destruction of the spirochætes. Yet, as recorded, within eighteen hours of an injection of but 0·3 grm. of salvarsan not a single *Spirochæte pallida* could be discovered in repeated examinations; and, moreover, the patch had healed by the following day. What is of even greater importance to my mind is the fact that not only did these drugs fail to influence in any way the clinical manifestations, but fresh lesions developed whilst the patients were undergoing treatment—namely, the ulceration of the fauces in one case, and the appearance of fresh papules in the other, in each of which *Spirochæta pallida* could be demonstrated. One of the greatest assets, from a sociological point of view, of salvarsan (and indeed of most of the other organic arsenical compounds now being substituted) is the rapidity with which the infectious lesions are rendered non-infectious. I have not been able to prove that ferrivine and intramine have any influence in this direction. If I had been able to prove that intramine and ferrivine were even superior in effect to salvarsan, neo-salvarsan, kharsivan, galyl, nov-arseno-benzol or luargol, yet would I hesitate to substitute them for any of these until they had been subjected to far more exhaustive trials, controlled by microscopical and serological findings, in several disinterested laboratories, *such* is the severity of the reactions, local and general, produced. With regard to the local effect produced by the intramuscular injection of intramine, I cannot do better than describe a case in which I opened an abscess resulting from the administration of this drug four weeks previously. The pain during the week following the injection was very severe: the patient, who was confined to bed, was unable to lie upon the side on which the injection had been made. Definite necrosis of muscle fibres had ensued—a well-defined cavity resulting—from which a yellow "mucoid" fluid was evacuated. There was no evidence of sepsis. A tag of partially necrosed fascia protruded from the incision. In three other cases in which the treatment with intramine was commenced at the same time as the case just described, absorption of the drug is not yet complete, as can be evidenced on palpating the site of injection. In each case two injections of 1 grm. were administered at an interval of a week. In every instance a definite "gap" can be felt in the body of the muscle where necrosis has ensued. I cannot attribute such unsatisfactory absorption in each of the eight injections to any error of technique. Each injection was made slowly and strictly intramuscularly, tension being avoided. Massage was employed for three succeeding days. In other cases necrosis has ensued in every instance, though fortunately the subcutaneous tissues and skin have only broken down in two instances. A discharging sinus still exists in the one, and has now remained obdurate for twelve weeks. I consider that apart from any toxicity that ferrivine possesses, the solution is far too acid to be put upon the market for indiscriminate administration to the public. I would like to mention, now, the cases which Mr. McDonagh has brought up for us to see this afternoon. In two of those cases one could definitely feel that the injection of intramine was encysted, and on puncturing same "mucoid" material would escape, as in our own experience with these residual abscesses. In another case, in which instance the patient has been under these drugs for over two months, and I presume to be shown because he is doing well, he has definite lesions on his fauces and an anal mucous patch. I feel positive that I could demonstrate the *Spirochæta pallida* from either of these lesions to-day. It was in this very room—less than four weeks ago—at the meeting of the British Ophthalmological Congress, that I was privileged to hear Mr. Ernest Lane's remarks upon his experience with these drugs in his wards at the London Lock Hospital. I need only state that his description of the reaction resultant upon the administration of intramine and ferrivine, local, general, and therapeutic, tallies with our own findings. If anything, he painted a darker picture.

Dr. C. H. **Browning**: On attempting to weigh the evidence which has been advanced this evening regarding the therapeutic effect of ferrivine, one is struck by the absolutely conflicting character of the statements. On the one hand, independent observation has confirmed the striking influence of the drug on the primary sore in cases treated by Mr. McDonagh himself; from the chemical standpoint it does seem remarkable that ferrivine, which from the formula given appears to be the iron salt of the well-known substance sulphanilic acid, should exert such a powerful specific action in syphilis; but still one must always be prepared for surprises in a field as yet so little investigated. On the other hand, several observers of great experience have shown that when administered by themselves in similar cases little or no therapeutic effect could be detected. As regards intramine, extended experience seems to have led Mr. McDonagh himself to modify his previous statement; at the last meeting we heard from him that interstitial keratitis yielded to intramine, and I think I expressed the general opinion of those present when I commented on the remarkable advance which this achievement signified. To-night, however, it appears that Mr. McDonagh has met with interstital keratitis which was resistant to intramine. It is evident that judgment on the therapeutic action of these drugs must remain in suspense until there has been a much more extended trial in the hands of a number of independent observers.

Sir **Malcolm Morris**: I have come here to listen rather than to speak. As I said at the meeting a month or so ago, I am under a grave responsibility at the present time, having been a member of the Royal Commission on Venereal Diseases, and having had to advise a Government Department as to the remedies that should be supplied throughout the country free of cost. I confess that to give up the remedy that has stood the test in tens of thousands of cases and to switch off to another which has so far been tried, as Mr. McDonagh says, in less than 300 cases, is a course which does not commend itself to me as rational or justifiable. He himself exhorted us, in the early days of salvarsan, not to accept that remedy until a sufficiently long experience should enable us to form a competent judgment of its merits. At that time he was very enthusiastic about salvarsan, and gave addresses in various parts of the country on its advantages; but he warned us not to be in a hurry to accept the results claimed for it. I would remind him of that now in connection with his own compounds. I have a perfectly open mind in the matter. If a new remedy were discovered to-morrow which would destroy or suppress the spirochæte without producing toxic effects in the patient I should be among the first to welcome it. But I know of no sufficient evidence that such a new remedy has been discovered. I wish Mr. McDonagh success in the future. I admire his energy and his abundant labours; but, as one much older than himself, I may venture, perhaps, to suggest to him the propriety of submitting his remedies to further tests, and not to press them upon the profession until he has obtained a much more considerable body of evidence of their value.

Mr. **John Ward**: I would like to add that I was asked by one of the most emininent bacteriologists in London to go and see the life-cycle of the *Spirochæta pallida* prepared by Mr. McDonagh, and, on behalf of the Crookes Laboratories, I went. I expected to find bits of stained protoplasm which might be found under conditions frequently associated with degenerative tissue. I do not know that I am particularly qualified, but we have over 25,000 stained, indexed, and numbered slides, and I was convinced that Mr. McDonagh's statements are correct and that he has the life-cycle of the *Spirochæta pallida*, as is represented by his slides. I do not see how anyone, looking at them from an unbiassed point of view, could possibly mistake them, nor could their appearance be likened to that of degenerative tissue. The stains employed, especially pyronin and methyl green, are not easy nor generally used, but when obtained the result is excellent and a brilliant example of the theory of staining. I am convinced that any bacteriologist who saw these slides and carefully followed the *modus operandi* of each stain employed could not come away without being convinced of the proof of this life-cycle. I am only too pleased to think its discovery was due to an Englishman.

The PRESIDENT: As the time at our disposal has expired I will not now detain you by any observations of my own on the subject which is before us except to say that, so far, my opportunity of forming a practical opinion on the use of the drugs that have been so well advocated by Mr. McDonagh is practically *nil*. For the treatment of syphilis I have employed neo-salvarsan and neo-kharsivan, until the introduction of galyl. Since then all my cases requiring intravenous injections have been treated with this agent, and the results have been very satisfactory. It will necessarily require a long observation of the relative value of these new agents before anything of the nature of conclusions can be arrived at And I feel confident that Mr. McDonagh, by the energy he has shown, the careful and detailed studies he has made, and the knowledge of chemistry he possesses, together with his desire permanently to advance the treatment of syphilis, will not fail to give the fullest consideration to the views and criticisms of other practical observers before his own final conclusions are made. In these important matters—so important, as you have heard, that Government action will probably be taken upon them—it is our bounden duty in the interests of the community to secure not merely what is good but that which is certainly the best.

Mr. McDONAGH (in reply): Mr. President and Gentlemen,—Before I brought up the subject it was universally thought that the action of salvarsan was a direct one upon the parasites, and that arsenic was an essential ingredient of the chemotherapeutic preparations. I venture to think I have conclusively proved that neither of these accepted opinions is correct. My object in introducing intramine and ferrivine was first to substantiate my theory of oxidation and reduction, and secondly to show that non-toxic elements like sulphur and iron have a therapeutic action in syphilis. Intramine and ferrivine were not introduced immediately to replace salvarsan and its substitutes, as both had disadvantages which required to be overcome. Intramine is painful, but the pain caused is nothing like so severe as that described by several of the speakers. From the accounts given of the pain and from the photograph shown it is perfectly clear that the best site for intramuscular administration of drugs is not so widely known as would be expected. No speaker has offered any suggestion for depriving intramine of this disadvantage. Ferrivine did at first cause shock in some cases, a difficulty now overcome, but not with help derived from the discussions. No suggestions have been offered *re* carrying out the improvements with ferrivine, which must be so clear to those who understand the foundation upon which chemotherapy is built. Unless I am able to get the necessary assistance in this country, I shall go abroad for it, since I am convinced that an improved iron compound will be invaluable in the treatment of syphilis. Concerning Colonel Harrison's remarks on the life-cycle, I would like to ask him if he has repeated any of the work. Two observers have done so on the Continent and confirmed my results. Because English biologists have not repeated the work is no argument against the correctness of mine; indeed, it is a sound argument in favour, since medical history has shown that the longer it has taken work to be accepted the sounder it is, and *vice versâ*.

EDITORIAL.

THE REPORT OF THE ROYAL COMMISSION ON VENEREAL DISEASES.

It is now some months since the Royal Commission on Venereal Diseases, appointed in November, 1913, issued its final Report. We have, therefore, had an opportunity of thoroughly considering its recommendations, and are also in a position to know what steps the Government proposes to take with regard to it; so that the time would appear to be appropriate to make a few remarks both on the Report and on the proposals of the Local Government Board.

Abstracts of the Report have been published in all the chief lay and medical papers, and we anticipate that most of our English readers have obtained the full Report and studied it for themselves. If they have not, we most heartily recommend them to do so, as the document is a masterly survey of our present knowledge of venereal disease and of its effects on the population. To give an adequate summary would be impossible in the space available, and as it is so easily accessible, would be a work of supererogation, but we propose to mention the chief conclusions arrived at.

It is not out of place in the first instance to consider how the appointment of the Royal Commission came about. For many years past medical men and social reformers, realising the havoc wrought by these diseases, have urged successive governments to inquire into their prevalence and to take steps to deal with them. In the middle of 1913 a letter, signed by a number of influential medical men, calling upon the Government to act, appeared in the daily press, and in August of that year, at a joint meeting of the Sections of Dermatology and Syphilography and of Forensic Medicine of the Seventeenth International Congress of Medicine, held in London, a strongly worded resolution in the same sense was passed. As a result of these appeals, supported by the energetic action of several gentlemen, among whom we may mention the President of the former Section, Sir Malcolm Morris, the Government appointed the Commission under the chairmanship of Lord Sydenham "to inquire into the prevalence of venereal diseases in the United Kingdom, their effects upon the health of the community and the means by which those effects can be alleviated or prevented, it being understood that no return to the policy or provisions of the Contagious Diseases Acts of 1864, 1866, or 1869 is to be regarded as falling within the scope of the inquiry."

The Commission commenced its sittings in November, 1913, and examined in all eighty-five witnesses, including several distinguished continental experts.

In general, the conclusions arrived at by the Commissioners are: That better results in the control of these diseases are likely to be obtained by the education of the public and the provision of adequate facilities for treatment than by such methods as registration of prostitutes or notification of venereal cases followed by compulsory treatment, as they believe that compulsion tends to the concealment of disease and often to improper treatment.

They find that the statistics available for a study of the incidence and effects of these diseases are very incomplete, though they are sufficient to demonstrate conclusively the dire results to the community; they, therefore, recommend that an effort be made to collect more statistical evidence, especially by the confidential notification of deaths, the extension of the Notification of Births Act, 1907, to stillbirths of under twenty-eight weeks, and for accurate returns of cases of venereal disease treated in institutions at public expense.

They consider that the prevalence of venereal diseases is in a large part due to the ignorance of the public on sex hygiene; they, therefore, lay great stress on education in sexual matters, and, while believing that it is not advisable to give detailed instruction of this nature in elementary schools, they recommend that private talks by head teachers to pupils leaving school should be general. They advocate instruction being given in continuation schools, workshops, and factories, and that students in training colleges should be prepared to enable them to deal with these subjects. They recognise that much of this instruction will have to be given—in the first instance at any rate—by voluntary agencies, and they recommend that the National Council for Combating Venereal Diseases should be recognised by the Government as an authoritative body for the purpose of spreading knowledge and giving advice in regard to questions of venereal disease in its varied aspects.

It is considered that if infected persons are encouraged to seek medical advice as early as possible, and if facilities for treatment are made available to the whole community at the expense of the State, the incidence of these diseases can be considerably reduced. In order to carry out these views, it is recommended that the larger local authorities should make arrangements with hospitals and other medical institutions in their areas to treat all comers free of charge, the cost being met by grants from Imperial and local funds in the proportion of 75 per cent. and 25 per cent. respectively. The Commisioners are satisfied that this can be carried out in existing institutions, and that no special hospitals will require to be opened; they also believe that the majority of hospitals will be willing to undertake the work.

While it is hoped that the provision of free institutional treatment will open up opportunities for treatment to the whole community, it is realised that many people who can afford to do so will still wish to be treated by their own medical attendant. The Commissioners in no way wish to discourage this, and they propose that facilities shall be afforded for pathological examinations to be made free of cost for practitioners who desire them, and also that, subject to proper safeguards, salvarsan and its substitutes shall be supplied gratuitously. They lay great stress, however, on the necessity for practitioners and students keeping themselves in touch with the most recent methods of diagnosis and treatment, and therefore recommend that they shall have free access to the clinics where these diseases are being treated. They further suggest that "questions relating to syphilis and gonorrhea shall be systematically set in medical and surgical examinations, so that the knowledge acquired in these diseases by candidates for examination may be tested."

In order to make patients realise the infectious nature of their disease and also the importance of regular attendance to obtain a cure, it is recommended that printed instructions should be given to patients attending doctors or hospitals, and suggestions as to the form of these instructions are made. Bound up with the question of regularity of attendance is that of selecting suitable hours for clinics, so that patients can attend without interference with their daily work, and to this end evening clinics are advocated.

The Commissioners realise the serious effects which may result from the treatment of venereal disease by unqualified persons and by quack remedies, and they strongly endorse the recommendations of the Select Committee on Patent Medicines that all advertisements of remedies for venereal diseases should be prohibited.

Further, the question of marriage of persons who have suffered from venereal disease is considered, and the Commissioners recommend that " statutory recognition should be given to the principle that infectious venereal disease constitutes an incapacity for marriage," and also that " the law should be amended to provide that a communication made *bonâ fide* by a medical practitioner to a parent, guardian, or other person directly interested in the welfare of a woman or man and with the object of preventing or delaying a marriage with a person who is in an infectious condition from venereal disease, shall be a privileged communication."

With regard to the notification of venereal disease, the Commissioners are of opinion that no system should be put into force at present, but that the question might be reconsidered when experience has been gained of the operation of the improved facilities for diagnosis and treatment already mentioned.

In giving an outline of the recommendations of the Commissioners, we fear that scant justice has been done to their Report, and we would repeat that we think all medical men should obtain it and study it in detail. Having had the opportunity of hearing the opinions of many persons who have studied the Report, we feel justified in saying that the recommendations are such as will appeal to the medical profession at large, and will obtain from them that hearty co-operation without which any attempt to make such a scheme workable would be brought to nought.

CIRCULAR LETTER FROM THE LOCAL GOVERNMENT BOARD.

Following the assurance given by the Prime Minister in the House of Commons, the Local Government Board have not been slow in formulating proposals for carrying out the recommendations of the Royal Commission.

In a circular letter dated July, 1916, and addressed to the Councils of the Counties and County Boroughs, to the Governing Bodies of Hospitals, and to Boards of Guardians, a memorandum is submitted, drawn up by the Medical Officer of the Board, Dr. Newsholme, who, it will be remembered, was himself one of the Commissioners, indicating the lines on which the Board proposes that the recommendations shall be carried out.

We propose to indicate the chief points in this memorandum, which we believe will in the main meet with the hearty approval of the profession. We must consider it from several points of veiw: Firstly, from that of the general public; secondly, from the point of view of the general hospitals, including the question of medical education; and lastly, from that of the medical practitioner.

General public.—It has been pointed out that in order to produce any marked effect on the incidence of venereal disease, it is essential that every encouragement should be given to the public to obtain early and thorough treatment. In order to carry this out, it is proposed that clinics should be established in each Administrative County and County Borough for treatment of patients in their areas, and that, as far as possible, existing hospitals should be utilised for the purpose. Further, that "every clinic should be available for the treatment of all comers without distinction as to means or as to place of residence." It is, moreover, proposed that clinics should be held at hours suitable to patients, so that they can attend for treatment without disturbance to their ordinary avocations, and that separate clinics be established for the two sexes. In view of the recommendations of the Commission, it is pointed out that absolute secrecy should be maintained about the patients' disease, and that, though the addresses of patients will be taken, they will never be communicated to others, but will be used purely in order to arrange subsequent appointments. Arrangements are also made by which private practitioners can have pathological specimens examined, and can obtain supplies of drugs at public cost, so that patients who prefer to be treated by their own doctors can be assured of having the most modern remedies.

As far as the public are concerned, we are of opinion that no stone has been left unturned to encourage them to obtain early and thorough treatment.

Hospitals.—We now turn to consider the suggestions made to the hospitals with a view to carrying out this scheme. Hospitals can, for practical purposes, be divided into two classes: (1) The large general hospitals with staffs of highly-trained specialists, which will include all the teaching hospitals, and (2) hospitals staffed by general practitioners and institutions with a whole-time personnel. As this Journal appeals chiefly to the specialist, we shall deal mainly with the application of the scheme to the former group.

It is proposed that hospitals shall enter into an agreement with the local authorities to undertake the treatment of venereal disease on the lines laid down in the memorandum, and that expenses incurred, such as payment of a medical officer to carry out this treatment, the supply of drugs and apparatus, and other necessary expenses, should be defrayed out of grants from Imperial and local sources. It is pointed out that, subject to the fulfilment of essential conditions as to treatment and as to returns, neither the local authority nor the Local Government Board desire to interfere with the administration of the hospital.

No hard and fast line seems to have been laid down as to the conduct of the clinic; two alternatives appear to be open, either the appointment of a whole-time medical officer, who will be responsible for the diagnosis and treatment of all venereal cases, or the appointment of a member of the visiting staff to the charge of venereal cases with the assistance of a whole or part-time paid medical officer. We believe that this is a very important point, but one over which differences of opinion may easily occur between the hospitals and the local authorities. For our part, speaking of our first group of hospitals, we think that a sufficiently clear distinction has not been drawn between the *diagnosis* and the *treatment* of venereal diseases. In a large hospital, however carefully cases are sorted out, a certain number of venereal cases are bound to distribute themselves among the different departments, and we believe that this is of great advantage, both to the patient, who obtains the best expert opinion on his case and incidentally is not labelled "venereal," and also to the student, who is able to see venereal cases side by side with non-venereal ones, and is, therefore, able to learn something of differential diagnosis. We think, however, that all cases of acute syphilis and venereal sore should be referred in the first instance to the dermatological department, and gonorrhœa in the male and female to the uro-genital and gynæcological departments respectively, as is being done in many of the leading hospitals at present. In all these departments arrangements should be made for the application of all modern methods of diagnosis, and they should be in close touch with the pathological laboratory.

Once a case has been *diagnosed* as venereal, it may well be transferred to a special department for *treatment*. It is of less importance whether that department is under a whole-time officer or whether one or more paid assistants should be appointed under the control of one or more members of the visiting staff. We incline to the latter arrangement in the teaching hospitals, as we believe that this will conform most to the constitution of these institutions. In the larger hospitals we think that one assistant should be appointed to carry out the treatment of syphilis and soft sore under the dermatologist, and another to carry out the treatment of gonorrhœa under the uro-genital surgeon and gynæcologist. In smaller hospitals one assistant could probably carry out the whole treatment.

There is still another class of acute gonorrhœa which must not be lost sight of, and that is gonorrhœal ophthalmia, a condition so serious as to be responsible for about a quarter of the cases of blindness in children. We are strongly of opinion that, although the actual treatment can be carried out by a junior officer, the best results will only be obtained when controlled by trained ophthalmic surgeons.

It may be argued that divided control will have a serious effect on the systematic carrying out of treatment and the preparation of statistics, but this difficulty can easily be got over by appointing one of these visiting officers to the administrative control of the whole treatment department and making him responsible for its proper organisation.

It must not be forgotten that many cases of chronic venereal disease which come to the hospital will require treatment, and that most of these will not in the first instance come to the departments mentioned above; it will, however, be of great advantage if the physicians and surgeons concerned can refer them to one department for treatment, but in order to have this carried out effectively it is essential that members of the staff should take the opportunity of discussing with the officer in charge of the clinic the line of treatment they wish to have carried out.

We cannot bring ourselves to believe that, in the great centres of medical education, it will advance the study of these diseases if both the diagnosis and treatment of syphilis and gonorrhœa are handed over to one whole-time official who will be so fully occupied with clinical work that his opportunities for research will be extremely limited.

In hospitals of our second group, namely those staffed by general practitioners or by whole-time officials, these considerations do not necessarily apply, and we consider that the appointment of one individual to carry out the diagnosis and treatment of venereal cases will best meet the requirements of the Royal Commission.

It is suggested that a small number of beds should be provided, and there will be no one who will dispute the necessity for in-patient treatment in certain acute venereal cases. The question as to whether every case in which salvarsan or one of its substitutes is injected should necessarily be detained for one or more nights is one in which considerable difference of opinion will be found.

It will be obvious that the proper carrying out of the diagnosis and treatment of venereal disease can only be accomplished by making full use of laboratory facilities and the services of skilled pathologists, and much of the memorandum deals with the arrangements which should be made for use of laboratories both by clinics and by practitioners. The special examinations required are: (1) Microscopic examination of discharges for the detection of gonococci, confirmed in exceptional cases by cultural methods. (2) Microscopic examination of discharges from sores, mucous patches, condylomata, etc., for the detection of spirochætes or of other organisms. (3) Wassermann tests on the blood-serum of patients, (*a*) for the diagnosis of syphilis, (*b*) as a control of the effect of treatment. (4) Examination of fœtal tissues for the presence of spirochætes. (5) More rarely Wasserman tests and microscopical examination of the cerebro-spinal fluid of patients.

It is pointed out that "the medical officer of a clinic may wish to undertake the microscopic examination for spirochætes and for gonococci, and may be competent to do so; and there are advantages, particularly in cases of suspected syphilis, in securing early microcroscopic examination of material"; but the memorandum goes on to say, "if the clinic and the laboratory are on the same premises or near each other, the need for making these microscopic examinations elsewhere than in the laboratory does not arise." In this latter view we do not concur; we are of opinion that it is most desirable that, where possible, the examination—at any rate of venereal sores—should be made on the spot, and that students should have the diagnosis confirmed or otherwise while the case is before them; for a report received after the case has gone loses a great deal of its educational value. Further, we think that it is most important that all students should become familiar with the methods of examining for spirochætes, and if examinations are only made in the laboratory there is considerable possibility of their being done by laboratory attendants. It is obvious that the Wassermann reaction must be done in the laboratory, and the whole profession will be grateful to the Government for making this test easily accessible to the practitioner.

Stress is laid on the importance of keeping accurate records of the cases treated in the clinics. Records should not bear the name and address of the patient, but be identified by a number. The name and address should be kept in a separate book, and should be treated as confidential, and only used for communications with the patient by the medical officer. Certain returns are to be made every three months to the Medical Officer of Health of the county with reference to the cases treated in the clinic during that period.

Medical practitioners.—We have now to consider how these recommendations will affect the practitioner. Probably the recommendation that gratuitous treatment will be available to all patients whatever their means will cause much criticism, and, on the face of it, not without some reason. In actual practice, however, it is very unlikely the bulk of patients who can pay for treatment will go to the hospitals, and it is doubtful whether practitioners will deal with any less number of cases than they do at the present time. Further, practitioners will now be able to give treatment, at the public expense, to those of their patients whom previously they had to refer to hospitals, for it is proposed that free supplies of salvarsan or its substitutes may, under certain conditions, be issued to practitioners, and that pathological examinations may be made for them free of cost.

With regard to the free issue of salvarsan, it is suggested that supplies should be obtained by practitioners from the medical officer of a clinic who has satisfied himself of the practitioner's skill in the administration of the drug. This provision will, we expect, raise considerable discussion, for it opens up an entirely new principle. It has always been accepted that a man who has obtained a medical qualification to practise is capable of carrying out any form of treatment, and we consider that the suggestion that practitioners should undergo a test at the hands of the medical officer of a clinic will be resented, and will often place the medical officer in a very equivocal position. We note, however, that in a recent letter from the Local Government Board this duty has now been transferred to the Medical Officer of Health. It must be clearly understood, however, that there is nothing to prevent a medical man carrying out any treatment he likes as long as he does not wish for a *free Government issue* of salvarsan, and that no restrictions are placed on the free use of pathological facilities.

We notice, with pleasure, that one London hospital at least has taken a step towards dealing with this problem. Thanks to the munificence of the Grocers' Company, who have built and equipped a ward for the purpose at a cost of £10,000, the London Hospital has opened beds for eight male and eight female patients for the treatment of syphilis. The ward is attached to Dr. Sequeira's skin-department, and has a well-equipped laboratory attached. The pathological side of the work is under the direction of Professor Bulloch.

ROYAL SOCIETY OF MEDICINE.

DERMATOLOGICAL SECTION.

MEETING held May 18th, 1916, Dr. J. H. STOWERS, President of of the Section, in the Chair.

Dr. E. G. GRAHAM LITTLE showed a case of *Parakeratosis variegata of the type described by Juliusberg as "Pityriasis lichenoides chronica."* The patient was a young girl, aged 18 years, one of three children, and the sole member of the family with any skin-disease. She had shown no signs of this until August, 1908, when she was spending a holiday at Felixstowe. During one night a vivid red rash appeared quite acutely on the legs and arms, which was ascribed to having bathed in the sea when the patient was hot. A medical man summoned immediately to see the patient seemed to have regarded it as possibly measles, although she had had this disease four years previously. From this beginning the eruption spread continuously but slowly, until within about two years the entire surface was affected, with the exception of the nails. The scalp was very scaly, but the hair had not fallen. Two years later, at the age of 13 years, she began to have epileptic fits, which had persisted up to now, and for these she was being treated with bromide. She began to menstruate when aged 11 years, three months before the rash appeared. There was, and had been, singularly little interference with the general health, and she had a good appetite, was well nourished and active, and slept well. She had no itching and had never complained of this symptom at any time; she was fond of, and had some skill in, painting and designing. The epileptic fits seemed to occur about the times of menstruation, which was normal and regular in frequency and duration. The fits were fairly controlled by bromide treatment, and she was enjoying longer intervals of freedom, intervals of four months being not uncommon.

In 1911 she was seen by his friend, Dr. Leslie Roberts, in Liverpool, who had been kind enough to send him this note of her condition when he saw her: "The patient, aged 14 years, was seen by me on February 24th, 1912. She was a very nervous person with a history of epilepsy. She was suffering from universal pityriasis. From my notes taken at the time I must have been under the impression that the disease was not the Pityriasis rubra of Devergie, but that it sprang from a seborrhœic base. The post-aural spaces were affected, and in the region of the forearms the disease was tending to pass into dermatitis. She also improved considerably under treatment between February 24th and May 15th, 1912. From these data I conclude that the disease in 1912 was not parapsoriasis."

Present condition: The eruption was very nearly universal, in the form at present of a fine branny lichenoid desquamation, with points of accentuated redness as compared with the bluish-red general tone, these points constituting a very indefinite maculo-papule. There was a shadowy effect of meshwork. The face was desquamating and red in blotches, not entirely all over. The palms and soles were hardened, the nails unaffected. Over the extensor surfaces of the joints, elbow, wrist, dorsum of hand, knee and ankle, there was much thickening, rather like that of Pityriasis rubra pilaris, but there was nowhere any resemblance to a follicular papule, so that this diagnosis could be excluded. The forearms and arms, from wrist to axilla, were especially bluish, almost cyanosed, but there were nowhere telangiectases. The mucous membranes were normal. The colour of the eruption seemed to vary, and at times assumed a vivid blotchy redness like measles, for which, in fact, as had been stated, it was mistaken at its inception. Silvery fine scales were freely shed, and in some positions, such as in the meatus of the ears, formed heaped-up masses which blocked the orifice. The thyroid was probably small and was not palpable. There were some enlarged glands in the neck. The teeth were very decayed and faulty. The pulse at the time of examination was 80, somewhat small and compressible. For the past two years she had used very persistently and freely an ointment containing 10 gr. of ammoniate of mercury to the ounce. Since the full development of the eruption—that was, since about the age of 13 years—there had been no change in the rash except, as had been said, that a certain vividness of colour might be added to the general prevailing bluish-red tint. No treatment, and she had had many forms of it, had made the smallest impression on the disease. The chest and abdomen appeared normal, and there was nothing to remark as to the urine.

The general facts in this case seemed to approximate it rather closely to the group of seven cases collected by Fox and MacLeod in their admirable paper on "Parakeratosis variegata," and classed by them with the "Pityriasis lichenoides chronica" of Juliusberg. The youth of the patient, the character of the eruption, with its resemblance to a receding Lichen planus, the wide distribution, the absence of constitutional symptoms, and the resistance to treatment, which were such noteworthy features of this case, were all reproduced in that series of seven cases. In one of that series, that reported by Jadassohn, there was a history of an almost equally sudden inception. With this exception he had not found any other instance in which an acute onset—so acute, in fact, as to suggest an exanthem to an experienced general practitioner—had been recorded in any of the somewhat dissimilar cases which were provisionally included in the category of Parakeratosis variegata.

Histological Note on the Case.—By the kindness of Dr. Staddon, of Ipswich, the patient's private practitioner, who performed a biopsy, he was enabled to add a note on the histology. The sections proved extremely hard and blunted several razors. There was a much thickened stratum corneum, the cells of which showed no deficient cornification and stained uniformly, no nuclei being seen. In several parts of the section there was free separation of thick stratified lamellæ of the stratum corneum, which was everywhere unusually dehiscent. There were especially numerous and abundant plugs of horn cells at the mouths of the follicles, almost recalling the appearances of Pityriasis rubra pilaris. The stratum lucidum was not detected, but as the sections were, as had been stated, very hard and difficult to cut, finer points of histology could not be very definitely made out. The stratum granulosum was deficient or more often entirely absent, being at the most represented by a single layer of cells. The rete was thinned and the interpapillary process practically non-existent, the papillæ being flattened out. There was some separation of epithelial cells (interepithelial œdema), and the inconspicuous demarcation between the epidermis and corium (the "blurring" of the basal layer) was a very notable feature. The localised papular character of the eruption was much more noticeable in the sections than would have been supposed from clinical inspection. In such localised areas there was a moderate cellular infiltration, probably mainly leucocytic, of the pars papillaris of the corium and perhaps some dilatation of the superficial vessels, but certainly not a conspicuous dilatation. The bundles of collagen seemed on the whole somewhat swollen, but there was no cellular infiltration, and below the level of the pars papillaris one could detect no abnormalities.

Sir MALCOLM MORRIS asked if there was anybody present who saw the four cases shown at the annual meeting of the British Medical Association in Edinburgh, one of which was exactly similar to this. If so, did any member know the subsequent history? From his knowledge of a limited number of these cases he would say that they went on for years, and then one lost sight of them, without learning the later history. They certainly did not get well from drug treatment in fact, he did not know that this even improved them. One would like to know whether the disease wore itself out. One of the four cases he spoke of turned out to be Mycosis fungoides. All four were Scotch cases.

Dr. PRINGLE stated that previously to that there were one or two cases shown at the old Dermatological Society of London by Dr. Payne among others. His impression was that these cases never got well, that the skin became atrophic, and the patients died ultimately of marasmus. In one case he had certainly seen that happen. No treatment seemed to be of any avail.

The PRESIDENT had recently had, privately, a case very similar to this, which Dr. Pringle was good enough to see with him, the patient being the sister of a medical man. The itching in his case was very continuous and severe, but in the patient now exhibited it was almost absent. It was remarkable how subjective symptoms varied in different people suffering from this rare disease. He agreed with the remarks made concerning treatment, but in his case a course of X-ray exposures lessened the cutaneous thickening where it was most severe and reduced the itching to such a degree that a life of distress became comparatively comfortable. The nails in his patient were slightly affected.

Dr. E. G. GRAHAM LITTLE showed a case of *Lichen scrofulosorum*. The patient was a girl, aged 13 years, who had been under the care of the Inoculation Department at St. Mary's Hospital for some two years for a scrofulodermia of the neck of five years' duration, resulting from a tuberculous glandular abscess, during which she had been having for most of the time small doses of tuberculin in the form of bacillary emulsion. She was sent to his department on February 17th, when he saw her for the first time, his opinion being desired on a new eruption which had come out suddenly. This consisted of a large number of patches (twenty-three were counted) of grouped follicular papules, the patches forming oblong or circinate shapes from 1 in. to 4 in. in diameter, and distributed on the back and front of the trunk at a level between the navel and the nipples. There was also a small single circinate patch in the right groin and another over the left shoulder. The papules were of a vivid red colour, not spiny, and at the periphery of the patches were somewhat more salient and more vivid in colour. No complaint was made of subjective sensations. There was no rise of temperature. The patches persisted with little change except that there was a slow but progressive fading of colour, so that the aspect at the time of showing the case was much the same as that described at its inception. At his suggestion the injections of tuberculin which she was having had been omitted until the date of the meeting, and this fact might partially explain the retrogression of the lesions.

The case was especially interesting in view of the recent papers contributed by Sequeira and Adamson to the *British Journal of Dermatology* in comment on the work of Rist and Rolland. The eruption was the most perfect example of the disease which he had seen since he showed a case almost equally typical at the Dermatological Society of London fifteen years ago,* a coloured reproduction of which appeared in the *Medical Annual* for 1908, p. 363.

Dr. J. H. SEQUEIRA remembered an interesting paper by Lessellliers,† in which he showed that the histology of the lesions of Lichen scrofulosis produced by the injection of tuberculin was identical with that of the lesions in a tuberculous person who had had no injections. He looked upon the present as a typical case following tuberculin injections. He had also seen cases from time to time in which tuberculin injections had produced other types of reaction in the skin: sometimes of the nature of Bazin's disease, sometimes of the nodular tuberculide type.

Dr. S. E. DORE did not think it necessarily followed that this eruption was due to tuberculin; it might possibly arise from the tuberculous lesion itself. Last week he saw a child with a large patch of scrofulodermia on the arm and a typical eruption of Lichen scrofulosorum on the trunk, and no injections of tuberculin had been given in that case.

Dr. PERNET said that although one had to think of the tuberculin as the possible cause of this Lichen scrofulosorum, he might state that a week or two ago he had a case at the West London Hospital, that of a child with Lichen scrofulosorum, and it had had no injections. All that could be found were enlarged glands in the neck.

Sir MALCOLM MORRIS remarked that these cases occurred long before tuberculin injections became the vogue.

Dr. GRAHAM LITTLE (in reply) said that the Inoculation Department at the Hospital had been giving tuberculin injections over a very long time in many types of disease, and it was very rare for such eruptions to occur during these injections.

Dr. E. G. GRAHAM LITTLE showed a case of *acute disseminated*

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* *Brit. Journ. Derm.*, 1901, xiii, p. 167.

† Leselliers, *Annales de Derm. et de Syph.*, 1906, p. 897.

Tuberculosis cutis. The patient, a male infant, aged 7 months, was brought to him on May 4th for his opinion on an eruption which had come out quite acutely about a fortnight before. When he saw it the whole of the skin from the buttocks to the feet was closely covered with an eruption of small, deep, bluish, nodular lesions varying in size from that of $\frac{1}{16}$ in. to $\frac{1}{4}$ in. The eruption was so closely set that one could not have put a threepenny-piece on the affected parts without obscuring several lesions. Above the level of the pubes the skin was unaffected. The child was under the care of his colleague, Mr. Kenneth Lees, who was about to remove some tuberculous glands in the neck. There was a sinus from one of these glands, and another from a necrosed area in the mastoid. The mother stated that the glands had become enlarged at the age of 2 months, and the mastoid had been operated upon for tuberculous disease of the bone at the age of 3 months. The eruption was not itchy at the time of the visit to him, and there was no scratching. The child looked desperately ill. It had been proposed to postpone the operation on the glands on account of the rash, but by his advice this was performed the following day, and about twelve glands, some already caseous, were removed. When seen a fortnight later, at the meeting, a remarkable change had taken place in the aspect of the eruption, which had faded almost beyond recognition; the blue nodules had disappeared or diminished to pale papules not unlike those of a papular urticaria, and there was now some itching, which had certainly been absent earlier. The child looked much healthier. A portion of the affected skin had been excised at the same time as the operation on the glands, and half of the specimen had been injected into a guinea-pig and half retained for histological examination. It was too early at present to make any statement as to the effect on the guinea-pig, but the section of skin had been examined. No bacilli were found in sections suitably stained. There was a deep-seated cellular infiltration in the corium in circumscribed areas constituting foci, but there were no giant cells. The cellular infiltrate consisted chiefly of mononuclear cells, with some large epithelioid cells; the histology was thus totally unlike that of an urticaria. The dramatic disappearance of the nodular eruption was remarkable, for it had not shown any resemblance to the papulonecrotic tuberculide, as there had been no necrotic summits to the papules after removal of the infected glands. Bacilli had been easily demonstrated in the sections of the glands removed, so that the tuberculous nature of these was undoubted.

The clinical and histological appearances of this case presented a remarkable resemblance to a case reported at great length by Pelagatti.* In this instance the patient was a male child, aged 2 years, and the eruption had covered nearly the same areas—that is, the lower limbs and lower part of the trunk. The papules were small hemispherical lesions with a scale or crust on the surface. The eruption had come out acutely, there was a widespread tuberculous adenitis, and the patient died about three months after the appearance of the eruption, and post-mortem examination showed the cause of death to be acute disseminated tuberculosis. Histologically there were the same focal infiltrations of cells, with, however, some giant cells, which were not found in his case.

Dr. GEORGE PERNET showed a case of *tertiary syphilis treated by intramine.* The patient was a woman, aged 30 years, who was first seen on March 3rd, 1916, for broken-down gummata about the lower extremities of three months' duration, and beginning below the left ligamentum patellæ. In front of the left patella there was a punched-out circular ulceration, with a larger and somewhat reniform ulceration below it. On the outer side of the right knee-joint, and a little above it, a smaller circular ulcerated area of the same type was observed. Lot. nigra only was ordered. On March 7th 8 c.c. of intramine was injected into the left buttock. The 10-c.c. syringe used was the one devised by Dr. Chatin, and made by Gentil, of Paris. This has an ingenious device for fixing the needle to the nozzle, and is supplied with a rubber piston worked on the Archimedean screw principle. On March 10th the patient stated she felt better, though there had been a good deal of pain for the first night after the injection. The buttock was tender and swollen. The lesions themselves were unchanged in appearance, but they were less painful, a symptom about which she had previously complained. On March 14th the patient considered the ulcerated areas were better, and she felt better in herself. Ung. acidi borici was ordered locally. On March 21st the ulcerated lesions were distinctly healing up; they were smaller and flatter. The left buttock had quite recovered from the injection; 7 c.c. of intramine were injected into the right buttock. On March 24th there was some hard swelling and redness about the seat of the injection and beyond as a result. Healing of the lesions was still going on. March 31st: Healing up well; pain from injection occurred as before. April 14th: Buttocks quite recovered. The greater part of the lesions on the left leg had healed up, but there were still some ulcerated foci about. The lesion on the right side almost completely healed up.

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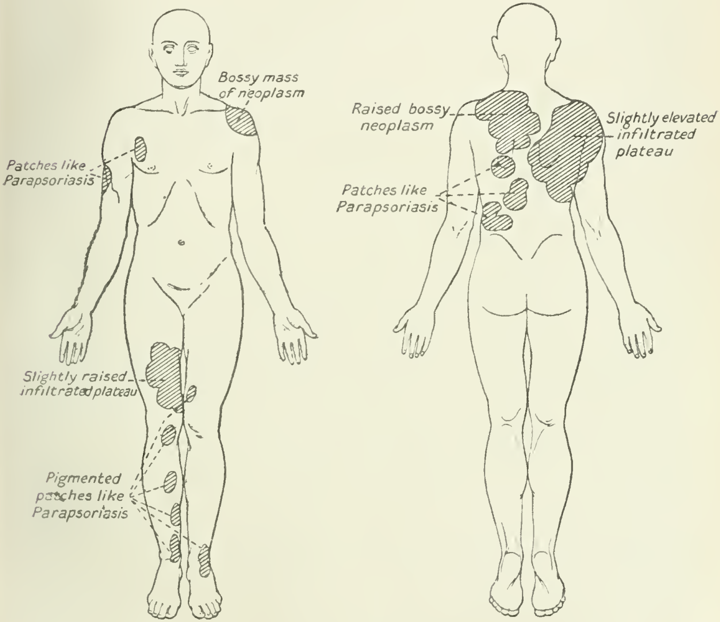
* Pelagatti, *Giorn. Ital. delle Malattie della Pelle,* 1898, p. 704 (with coloured plate of histology).

As there was no clinical meeting of the Section in April, the patient was put on iodide of potassium 5 gr. ad 1 oz. t.d., p.c., and she had been taking this up to date. There were still one or two small superficially ulcerated foci on lesions on left leg.

This case showed that intramine would lead to healing of syphilitic ulcerated lesions, but compared with arseno-benzol and galyl intravenous treatment it was slower. There was also the question of pain with intramine. This patient was exceptionally good about it, and readily agreed to the second injection. But that would not be the case probably with most patients, especially those who have to earn their living by laborious work as was usual with hospital patients.

A point of some interest in this case was that four years previously she had attended the Gynæcological Department of the West London Hospital for soreness of genitalia. On looking up the case it was found she had been under Dr. Simson, who noted she had what looked like a primary sore, which he had confirmed later by a positive blood test. She had one intravenous injection of salvarsan at the time (four years ago that was) and no other antisyphilitic treatment since. She was no doubt "whitewashed," and never turned up again —as occurred so frequently among out-patients—until she came under his care last March. The fact was that the very efficiency of salvarsan and other similar bodies in clearing up early symptoms rapidly was a disadvantage in dealing thoroughly with syphilitic cases. It need not be said that this case would be followed up with mercury treatment.

Dr. J. J. Pringle showed a case of *Mycosis fungoides in a woman.* The patient, S. S—, aged 43 years, was the wife of a railway platelayer. She had lived at Hatfield (Herts.) for the last seventeen years, and all her previous life in Leicestershire. She was of more than average intelligence. She had had four healthy children, and subsequently one miscarriage (at the sixth month), six years ago. About the same time she observed a "brown patch" on the inner side of the right thigh, which had persisted ever since. Her attention was drawn to it by itching. The patch gradually spread, but the condition remained limited to the right thigh for two years. Four years ago large brown patches appeared over both scapular regions, and several others over the rest of the back, but no definite dates could be assigned, and apparently little significance had been attached to them. The first "lump" appeared in the left supraspinous fossa about two years ago. The accompanying very rough diagram, made on admission to the Middlesex Hospital on April 14th, indicated the distribution of the lesions. The only one of these exhibiting distinct tumour formation was situate on the left upper scapular and supra-


Bossy mass of neoplasm
Patches like Parapsoriasis
Slightly raised infiltrated plateau
Pigmented patches like Parapsoriasis
Raised bossy neoplasm
Slightly elevated infiltrated plateau
Patches like Parapsoriasis

spinous regions, which were occupied by soft, bossy, pale pink, almost gelatinous masses projecting more than ½ in. above the general skin level. The surface of these masses was superficially eroded, and from it a thin, clear, sticky fluid exuded. The dimensions of this tumefied patch were 7 in. by 9 in. A rather larger composite patch was situate over the left shoulder and scapular regions; and although it was very superficially eroded and moist it was not prominent and showed no actual tumour formation. The original patch on the inner side of the right thigh presented identical characters. All the smaller isolated patches presented to a very remarkable degree the characteristics of Parapsoriasis en plaques; many of them were accurately oval or circular; their colour was deep brownish-yellow; their surface was distinctly lichenified and slightly scaly; their outlines were regularly convex and festooned where they had become confluent, and the borderline between healthy and diseased skin was remarkably clearly defined. At no point was any induration palpable to touch. The spleen was not enlarged, and there was no augmentation in size of any of the superficial lymphatic glands. The blood count was as follows: Hæmoglobin, 90 per cent.; red corpuscles, 3,250,000 per cubic millimetre; leucocytes, 4400 per cubic millimetre. Differential count: Neutral polymorphonuclears, 46 per cent.; lymphocytes, 33 per cent.; transitional and hyaline cells, 10 per cent.; eosinophile polymorphonuclears, 1 per cent. No abnormal forms seen. The chromatocytes showed no notable abnormality, either as regards morphology or staining reactions. The Wassermann reaction, tested on two occasions (Dr. C. H. Browning), was strongly positive. There were no other signs or symptoms suggestive of syphilis, except the history of a miscarriage at the sixth month (previously referred to).

The large granulomatous patch was exposed to a full unscreened pastille dose of X-rays on April 16th, and its characters had been totally changed for the better; its surface was seen to be flush with the surrounding skin and was almost uninterruptedly epidermised. All the other patches had been subsequently exposed to the same dose of X-rays or to the mercury-vapour lamp, but the results were not yet equally manifest. It had not been possible to make any histological examination.

The points in the case to which he specially drew attention were:

(1) The pure "Parapsoriasis en plaques" type of the primary lesions without erythrodermia.

(2) The unusual "gelatinous" character of the only mycosic growths which had so far developed. (This could not be demonstrated at the meeting.)

(3) The positive Wassermann reaction.

He hesitated to make the almost inevitable deduction from this fact in view of the absence of other confirmatory signs of syphilis; but he thought (illogically perhaps) that it gave him some justification for testing the value of galyl, which he proposed to use, or one of the other arseno-benzol series. He was aware of the disappointing results reported by a few who had given these substances a trial, but no great or convincing amount of evidence had been adduced one way or the other.

Dr. J. H. SEQUEIRA asked Dr. Pringle whether he laid particular stress on the fact that the Wassermann reaction was positive; whether in that statement there was a suggestion that Mycosis fungoides in a non-syphilitic subject might give a positive Wassermann reaction just as cases of lepra might. In a collection of cases which he made for a paper he read there some time ago, in a small proportion of cases there was a definite history of syphilis, and in some the Wassermann reaction was positive. He did not find sufficient evidence to consider syphilis an ætiological factor, as most cases gave a negative Wassermann reaction.

Dr. GRAHAM LITTLE said that members might be interested to hear that the acute case of this disease which he showed and reported last year died a few weeks after exhibition. On the recommendation of a number of speakers at that meeting treatment with X-rays was continued, but with no diminution of the activity of the disease.

Dr. PERNET did not think this case was syphilitic, although the Wassermann reaction was positive.* He had seen a good many cases of Mycosis fungoides, but only one or two in which salvarsan had been used. He did not think 0·3 grm. of galyl would do any harm, and it might do good. He considered the case was undoubtedly one of Mycosis fungoides. In any case of Mycosis fungoides *à tumeurs d'emblée*, he was inclined to think the salvarsan did more harm than good.†

Dr. PRINGLE (in reply) said that he laid stress on the fact that the Wassermann reaction was positive in this case in order to elicit, if possible, the experience of others. He had no opinions to offer on the point, but he believed certain conclusions had been drawn by others. He proposed to treat this patient with salvarsan or galyl. He was aware that the effect of arseno-benzol compounds in such cases had been stated to be unsatisfactory, but what Dr. Sequeira had said seemed to give tangible grounds for such treatment.

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* Pernet in "Discussion on Mycosis Fungoides" (thirteen cases), *Brit. Journ. Derm.*, 1914, xxvi, pp. 260 *et seq.*

† Pernet, "A Case of Mycosis Fungoides d'Emblée treated Unsuccessfully by Salvarsan and X-rays" (International Congress, London, 1913).

Dr. DUDLEY CORBETT showed a *case for diagnosis* (? *Lymphangitis*). The patient was a clerk, aged 47 years. Ten months ago he was admitted to St. Thomas's Hospital suffering from a fungating carcinoma of the scrotum. Most of the latter, together with the inguinal glands on each side, were removed; suppuration inevitably followed, but he was discharged to a convalescent home with all the wounds soundly healed. Shortly after his arrival there a red patch similar in character to those now visible appeared on the anterior aspect of the left thigh. It rapidly faded, but left behind a discoloration, which had persisted to the present time. On examination one found a large oval patch, purplish in colour. On pressure this faded completely, leaving no staining, and returned when pressure was removed. Just below and to the inner side of this were some definite nævoid vascular tufts, not in any way resembling varicose veins. Three days later a similar red patch appeared on the left buttock. It was slightly raised, diffuse, with no definite margin, and was hot but not tender to the touch. There was no œdema. In two days it had now faded, leaving behind the same kind of purplish patch already described. Further red patches had appeared in this interval on the right buttock and on the upper part of the right thigh, and the patient felt ill. There was no external septic focus visible. He regretted that owing to the short time available he had been unable to investigate the case further. On the evidence at hand he could not account for the condition, and would be glad of suggestions as to the diagnosis.

Dr. G. PERNET suggested that possibly these manifestations were connected with the fact that he had had many glands removed from the upper part of the thigh and inguinal region in the operation; indeed, that was the *fons et origo* of the condition; there was an interruption of the lymph circulation. He did not know whether Dr. Pringle remembered seeing at the last Berlin Congress a man who had had his inguinal glands removed on both sides, and who had a severe lymphangiectatic condition about the scrotum in consequence. In cases of elephantiasis due to filarial disease there was a similar blocking. Such patients were liable to erythemato-inflammatory attacks in the skin of the affected leg, with febrile manifestations.

Dr. J. H. SEQUEIRA asked if the temperature was raised. This kind of ymphangitis was not uncommon after extensive breast operations. Mr. Sampson

Handley had called attention to the subject. In some cases it went on to *cancer en cuirasse*, a blocking of the lymphatics by recurrent attacks. He thought the veins were also affected.

Major Gray thought this condition had a very direct connection with the removal of glands at the operation. The case presented a most remarkable picture of the anatomical distribution of the lymphatics which drained into the glands in the groin. Speaking from memory, the glands in the groin received lymphatics from three areas: the inner group from the front of the thigh, the middle from the lower abdomen up to the level of the umbilicus, and the outer from the buttock. In this patient the lymphatics of the inner and outer groups —namely, on the thigh and buttock—were involved, but those of the abdominal or middle group were not affected. He considered the condition was a lymphangitis, but he could not say why the abdominal area was not involved, except possibly that there was a freer anastomosis of the lymphatics there, so that they had not been blocked in the same way. With regard to Dr. Sequeira's suggestion that this might be an early stage of *cancer en cuirasse*, he thought that was scarcely tenable here, because the patient had had the condition on the left side and this had cleared up, which he did not think ever happened in cases where the lymphatics were blocked with cancer cells. He regarded this as a lymphatic obstruction of inflammatory origin. What the organism causing the trouble was, or how it got there, was another problem. He believed that the dilated venules were the result of a vascular obstruction which one often saw associated with a chronic œdema.

Dr. J. H. Sequeira (in reply to Major Gray) said that he did not suggest this was *cancer en cuirasse*; he simply said that it had been shown that lymphatic obstruction was a cause of *cancer en cuirasse* where there was malignant disease of glands.

Dr. Dudley Corbett showed a case of *Asphyxia reticularis* (*Unna*). The patient was a woman, aged 31 years. Two years ago she was engaged in laundry work, but had done no similar work since that time. Though naturally she worked in a hot atmosphere she was never exposed to the direct heat of a furnace, nor did she now make a habit of sitting unduly close to the fire at home. Twelve months ago the present condition appeared on the outer aspect of left leg, and nine months ago on the right leg. On the former it consisted of a strongly marked venous network, the meshes of which had a diameter of about $\frac{3}{4}$ in., it was of a dark purplish colour, and in places there were the remains of small bullæ, which appeared from time to time and broke down. On the right leg the process was less advanced, and there were no bullæ. There was a certain amount of irritation and a good deal of aching pain constantly present. He had called the condition Asphyxia reticularis, but he might perhaps have used the term "livedo annularis." He would be glad to know something of the pathology of the condition and the nature of the inflammatory or degenerative condition of the veins. Did it end in fibrosis with visible scar formation or did it ultimately disappear entirely?

Dr. GRAHAM LITTLE thought this must fall into the Erythema ab igne class. The distribution on the aspect of the leg which would be most exposed to a source of heat with the legs crossed was very characteristic. The causation was often ignored by the patient and might be quite trivial. The ridges marking out the meshes in this case were certainly unusually prominent, but they had all seen degrees of this, and Sir E. C. Perry * showed a case in which this feature was exaggerated. He had recently under observation a girl with a very similar appearance of the legs, and here the ridges slowly disappeared after some months. He thought the same result would follow in this instance. He certainly did not think it could be called an Asphyxia reticularis of Unna, in which, if he remembered right, ulceration was present. He showed a case with this label at the Dermatological Society of London in 1903, which apparently accepted this diagnosis, and he had a water-colour drawing of it. Ulceration was a prominent symptom.

Mr. SAMUEL thought this was possibly a case of Lichen planus taking on a peculiar pattern. Some time ago he showed there two sisters with Lichen planus. One of them presented a condition very similar to this. It was agreed by members present that it was Lichen planus, as she had typical Lichen planus elsewhere. On the legs there was the same reticular formation. Some of the papules in this case were shiny and of a violaceous tint.

Dr. J. M. H. MACLEOD suggested that the case might be one of Lichen planus reticularis, as there were certain shiny, violaceous, obtuse papules towards the lower part of the lesion which somewhat suggest that diagnosis.

Dr. H. G. ADAMSON said that in spite of the fact that the patient denied exposure of the legs to heat, he regarded this as an example of "Melanodermia reticularis," the result of "Erythema ab igne." The long hours of standing at her work would be a contributory factor. The fact that the inner side of the left leg was more affected than the right suggested that when she did sit by the fire she sat on the right-hand side, and this she admitted. He did not think that Unna's name of "Asphyxia reticularis," which was applied to a unique case, should be used to describe this more ordinary affection. He agreed with Dr. MacLeod that the eruption of Lichen planus often followed the network of livedo, but he did not consider Dr. Corbett's case an example of reticular Lichen planus. Very interesting reticulate eruptions were those in which syphilides and tuberculides followed this pattern, as in the Livedo racemosa syphilitica of Ehrmann and in certain examples of Bazin's disease; but this case did not belong to these.

Dr. PERNET considered the case was one of Erythema ab igne. With regard to the Lichen planus suggestion, he would point out that there was mild reticulation on the right leg too, but there were no signs of Lichen planus-like lesions in that situation.

Dr. F. PARKES WEBER thought the important point in this case of reticulate

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* Perry, *Brit. Journ. Derm.*, 1900, xii. p. 94.

erythema and pigmentation of the legs was the one alluded to by Dr. Adamson, namely, that as the exciting cause they had a combination of venous congestion owing to the dependent position of the lower extremities and a certain amount of hyperæmia due to heat—probably to sitting before a fire, as in most cases. The facility with which Erythema ab igne could be artificially produced varied perhaps in different persons, but amongst his hospital patients the frequent local application of heat (hot fomentations, hot indiarubber bottles, etc.) to the back or abdomen, for the relief of pains, had often sufficed to produce considerable and typical reticulate erythema and pigmentation exactly resembling ordinary Erythema ab igne. Ætiologically, this kind of reticulate erythema should be distinguished from the various forms of reticulate livedo, which it somewhat resembled.

Major Gray remarked that there seemed to be some tendency in certain individuals to get this particular kind of pattern. Some years ago he examined a good many school children, and if one put a row of boys, stripped, in front of a hot fire awaiting examination, about one in ten would get redness in this reticulated pattern instead of a diffuse redness.

Dr. Corbett (in reply) said he thought the position had much more to do with it than the heat, because he had already asked her whether she was near the fire in the laundry, and she said she was not. He thought that if there was anything in the history to account for the condition, it was the prolonged standing at her work, for there were some varicose veins. He could not agree that heat had much to do with it, as he particularly asked her whether she was near the fire at the laundry, and she had assured him that she was not, nor had her legs ever been unduly exposed to heat.

Dr. J. J. Pringle showed a case of *extensive carcinoma of the face occurring in the course of a Xerodermia pigmentosa; treated by a massive dose of radium.* This patient, a male, was previously exhibited on March 19th, 1914, and reported, with photographs.* He then had a huge ulcerating carcinomatous mass of the left cheek, involving the maxilla and extending as far back as the zygoma and ear, into which mass three tubes, containing in all 152 mg. of pure radium bromide, had been introduced and maintained in position for twenty-one hours. The remarkable improvement reported in 1914 persisted, but at the end of 1915 some recurrence had taken place at the inner portion of the growth, and on admission to the Middlesex Hospital three weeks before present exhibition a large, soft, ulcerating mass completely blocked the left nostril, and projected from it for a distance of more than ½ in. It had been treated with a tube containing 50 mg. of pure radium bromide plunged deeply into it and kept *in situ* for twenty-four hours. The result had been immediately and greatly beneficial, and the growth had shrunk well inside the aperture of the nostril.

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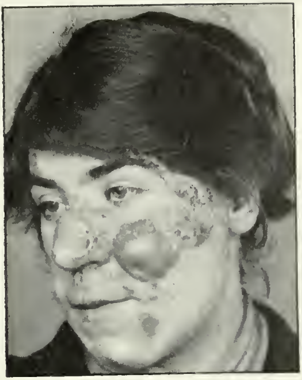
* *Proc. Roy. Soc. Med.*, 1914, vii (Derm. Sect.), pp. 130 *et seq.*

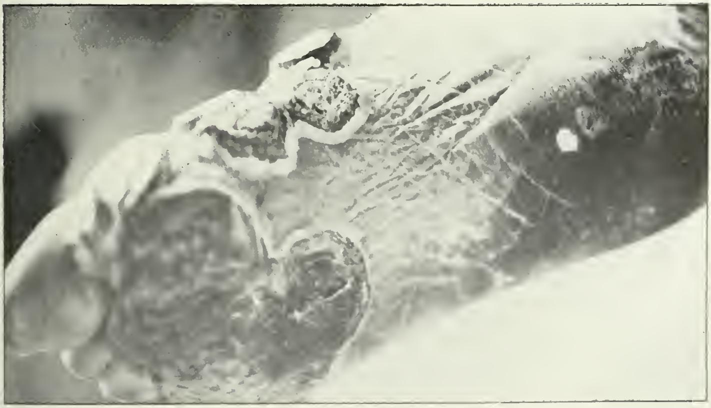
Dr. J. H. Sequeira showed a *severe case of acne.* E. P—, aged 20 years, a dressmaker, was admitted to the London Hospital on account of severe acne on March 7th, 1916. The skin was said to have been quite clear until three years ago, when the face became gradually covered with "blackheads and pimples." Large pustles formed later, but the inflammatory condition gradually subsided during the next year and a half. In December, 1915, the face again became very inflamed. On admission, the condition depicted in the photograph was present; the abscesses were of an unusually large size, and there were numerous comedones. It was remarkable that the eruption was limited to certain areas, and that the adjacent parts were absolutely free from any lesions. The patient had suffered from indigestion for many years, and four years ago was in a provincial hospital for goitre. The large abscesses had been evacuated and treated on general principles. The pus had been examined several times, and had been found to be sterile. The patient had not been taking either iodides or bromides.

Dr. George Pernet showed a case of *congenital Urticaria pigmentosa.* The patient was a male infant, aged 7 months, first seen at the West London Hospital on April 14th, 1916. The case was a typical one, the body generally (head, body, and limbs) exhibiting the characteristic pigmented spots of the complaint. On stretching the skin over them the yellow tint of the lesions was well brought out. The child was otherwise a healthy-looking baby, the only trouble he could find being that the motions were very dark. The lesions were extremely irritating, and kept the child (and its parents) awake at nights. The mother was not suckling the infant, which was being, therefore, artificially reared on a diet including groats. These had been knocked off. Carbonate of magnesia and soda, and a lotion of sanitas (1 in 8) had been ordered to be pressed in locally to irritating lesions. Since the applications had been made the infant had greatly improved all round. The lesions reacted in the usual way to pressure with the nail.

The congenital nature of this case had been purposely emphasised in the title. It was the grandmother who brought the baby to his



DR. J. H. SEQUEIRA'S SEVERE CASE OF ACNE



DRS. GRAHAM LITTLE AND HAYNE'S CASE OF KERATODERMA BLENORRHAGICA.

clinic. She was present at the confinement, and noticed the spots on the infant at the time of its birth, so there was no doubt about it. The parents, who had not been seen by him, were said to be quite healthy. No history of a maternal impression, such as seeing a leopard or dreaming of a leopard's skin, was forthcoming.

The PRESIDENT had a case under observation of very much the same kind The probability was that with care and dietary such complications would pass away.

Dr. MACLEOD said that one of the most interesting features of the case was that the condition was noticed at birth, as in all the cases which had been under his observation it had not appeared till some months after birth.

Drs. E. G. GRAHAM LITTLE and P. A. HAYNE showed a case of *Keratodermia blenorrhagica.* This case, which appeared on the agenda paper for exhibition, proved at the last moment too ill to be moved from St. George's Hospital, where he was under the care of Dr. Cyril Ogle, who had very kindly given them permission to report it.

The patient, F. W—, was a married man, aged 56 years, a leather-worker by trade, but his occupation for the past fifteen years had entailed no manual labour, as he had been a directing foreman.

Previous history.—He took venereal risks somewhat freely from about the year 1886, but had no apparent symptoms of infection until 1889, when he developed urethritis, followed by an arthritis of the left knee, and had an eruption of warty brown excresences which he recognised as the same lesion as was now present, but with a much scantier distribution, for they were restricted to two lesions on the left foot and three lesions on the right foot. They were "as big as buttons," and "dropped off" in the same way as the present limpet-like growths were wont to do. He seemed to have slowly developed a stricture, and to have had a severe urethritis in 1896, when there was a free discharge. In 1913 he again had severe urethral symptoms, including discharge, scalding, and pain, with scanty water, but these symptoms, with the exception of the discharge, had been more or less present for many years. At the end of November, 1915, he again noticed some discharge from the penis, in the form of "white beads" after micturition, and then for the first time began to feel seriously ill, and gradually "wasted to a skeleton." He had arthritis of several joints, the left knee, left foot, right knee and right foot becoming affected in that order. He was confined to bed, for the first time during his adult life, in the first week of January, 1916. About four weeks later, while still keeping his bed, the eruption made its appearance in the form of hard, waxy, brownish-yellow "scabs," which he had not seen since 1889, although he had had several attacks of urethritis, some attended by arthritis.

Present condition.—The man had a profoundly cachectic aspect, with the peculiar "fade" odour of chronic septic conditions, was much wasted and very feeble. His voice was weak and soon got tired. He lay motionless in his bed, on his back for the most part, and his muscular system was generally impoverished. He had difficulty in turning on his side or front and had to be helped in making these movements. The skin was universally dry, thinned, and of an "old ivory" colour. In addition to the arthritis of the knees and feet the middle joint of the right medius finger became acutely swollen and red on May 9th, but subsided somewhat rapidly after an injection of half a million gonococcal vaccine, given on May 10th for the first time, and repeated on May 15th. Condition of the skin: The chief incidence of the eruption was on the soles of both feet, which had been occupied with a very heaped-up mass of hard, horn-like material, as was well shown in the photograph. This had, however, now been largely shed, leaving a reddened dry scaly surface with a sharp line of demarcation from the healthy skin. The affected area encroached on the dorsum of the foot as well as occupying the whole sole, and at the upper line of the diseased skin nodules of waxy material were again forming on the reddened margin. There was a small brown mass on the front of the leg, about mid-way up the anterior aspect, and a larger but similar mass in front of the right knee, and also in front of the left knee. There were some small reddened areas the size of a sixpence on the anterior surface of the right thigh, which had been covered with brown waxy masses, but these had been shed. At the summit of the internatal sulcus there was a large suppurative lesion, perhaps caused by the weight of the body lying for so long in one position. There were three small brown heaped-up masses at the back of the right elbow, and along the outer and interior surface of the left forearm there were some small brown nodules. In both palms, but especially in the left, there was a coarse brown desquamation, and there was a similar small patch in the hollow of the umbilicus. Dotted freely over the scalp, which was quite bald except at the sides, there were several small limpet-like brown masses, with a base of the size of a threepenny-bit, and a conical waxy mass protruding from it to the height of about $\frac{1}{4}$ in. Nails: The patient had never shed his finger- or toe-nails. Some of the toe-nails were thickened, but not more than was usual with people who do not tend them particularly carefully; the thumb-nail of the left thumb was thickened at the distal end. The remainder of the finger-nails were normal and in good condition. Urine: Showed flocculent precipitate and threads. Weight: 5 st. 10 lb. Height: 5 ft. 6½ in. Material from the brown waxy masses was teased out and examined for bacteria. No gonococci, but some staphylococci were found.

The following notes have been contributed by Dr. Hayne, District Medical Officer of the Burma Railways Company, now on leave, who had been in charge of the case under Dr. Ogle since admission. They had to thank Mr. Hamilton Beattie, of St. George's Hospital, for the excellent photograph.

"Condition on arrival at St. George's Hospital (March 17th, 1916): An extremely ill, pale, emaciated-looking man; lips dry, tongue dry and coated, breath very foul, teeth dirty, gums of both upper and lower jaw puffy and swollen, with pus exuding from them. The whole trunk very emaciated; skin dry and rather yellowish. Heart and lungs: Nothing abnormal detected. Abdomen: Nothing abnormal detected. Joints: Both knees swollen; in colour waxy-white with dilated veins coursing over them; hot to the touch; a small quantity of fluid can be demonstrated in both knee-joints without causing much pain, and the majority of the swelling seems to be due to a general thickening of the tissues immediately surrounding the joint; they are extremely painful on passive movement; no creaking felt. Both ankles are swollen; the skin over the external malleoli is dusky red, but over the rest of the joint white; there is some fluid in both these joints, extremely painful on passive movement, but not on examination without movement. Hip-joints: There is no swelling or redness over either hip-joint; there is pain on passive movement; no creaking. No other joints affected. Pulse 120, temperature 99° F., respirations 17. Urine: Specific gravity 1020, reaction acid; no flakes floating about; no deposit; albumin and sugar *nil.*

"Family history: Nothing important; wife has had four children (youngest aged 10 years) and two miscarriages. Alcohol: Moderate during the last ten years, but has, as a younger man, had bouts of fairly heavy drinking (spirits and beer).

"During the seven and a half weeks patient had spent in this hospital the chief points of importance are that—

"(1) He still looks extremely ill, but that he eats and sleeps well and his general condition now is much the same as on admission.

"(2) The condition of the gums responded very rapidly to treatment, and are now no longer swollen and no pus can be pressed from them.

"(3) The condition of the joints is much the same, except that the fluid has disappeared from the knee-joints and there is less pain on passive movement and movement is less restricted. Ankles and hips as on admission. On May 9th the middle joint of the left fourth finger became red and swollen, but was quite painless to touch on passive movement.

"(4) A specimen of blood was taken, and on examination gave a negative Wassermann reaction. A specimen was taken from the serum under the crusts of one of the cutaneous lesions on the scalp, and showed staphylococci microscopically, and on culture media *Staphylococcus albus* was isolated.

"(5) Urine on weekly examination has not contained albumin or pus, except on May 20th, when it was noticed to contain some shreds and flakes of (?) mucus; there was a trace of albumin, and on microscopical examination there were a few polymorphonuclear cells, epithelial cells, and structureless-looking matter, probably mucus. No discharge could ever be obtained from the urethra. No bacteriological examination of the urine was made.

"(6) Pulse-rate varies between 120 and 130 or higher per minute, sometimes regular, sometimes irregular. Temperature variable, usually ranges between 99° F. and 100° F.

"(7) At the beginning of May a small subcutaneous abscess developed in the region of the tip of the coccyx, now almost dried up.

"Treatment: Local treatment to gums and cutaneous lesions. Tonics (quinine, arsenic, and iron) internally. April 28th: Massage was commenced to knee-joints and continued until May 10th. May 10th: Gonococcal stock vaccine, ½ million units (slight reaction). May 15th: Gonococcal stock vaccine, ½ million units (no reaction). May 20th:

Gonococcal stock vaccine, 1 million units (no reaction). May 25th: Gonococcal stock vaccine, 2 million units."

MEETING held June 15th, 1916, Dr. J. J. PRINGLE, Vice-President, in the Chair.

Mr. J. E. R. McDONAGH demonstrated *a new test for syphilis* (*the Emulsoid-gelation or Gel test*).—His research work had led him to look upon the serum as a colloidal system in which the protein particles form the "solid" or internal phase. The particles were emulsoid—*i.e.* they were partly in solution—therefore they contained water. The particles in a syphilitic serum differed from those in a normal serum. The size and number of the particles in a syphilitic serum were greater than those in a normal serum—a fact that could be easily proved by examination under the ultra-microscope; but as this method was not always available, he had proved the point in other ways. A syphilitic serum contained more protein nitrogen than a normal serum, more adsorbed amino-groups, and more adsorbed electrolytes; note the readiness with which syphilitic sera clot. None of these methods could be used as a routine for examining sera, so he undertook further experiments, and to-day he had the pleasure of exhibiting before them his new test for syphilis.

So long as the particles were in "solution" it was naturally impossible with the naked eye to distinguished one kind of serum from another, but if the colloidal form of the particles could be changed and an electrolyte used for their precipitation, to distinguish sera which contained varying quantities of protein would be a simple matter. In order to bring this about he employed glacial acetic acid, which threw out the protein as a gel. The presence of the gel could be made still more apparent by the addition of the sulphate anion, since the gel as it existed in an acid medium would have a positive charge. Thinking that that sulphate anion would have the greatest precipitating action which was the salt of a heavy metal, he chose lanthanum sulphate. At first he thought the changes which resulted from adding glacial acetic acid lanthanum sulphate was a transformation of the protein particles from the emulsoid into the suspensoid state, hence he called the reaction the emulsoid-suspensoid reaction, or, briefly, the E.-S. test. As the precipitate formed by the glacial acetic acid lanthanum sulphate was soluble in water and reversible, he presumed the changes which occurred were those of gelation.

Whatever was the more correct explanation of the changes which took place, there was no doubt that, by adding glacial acetic acid to very small quantities of serum, a syphilitic might readily be differentiated from a normal serum by the degree of the opacity caused and the rapidity with which a precipitate formed. The differences could be made more apparent and be produced more rapidly by the addition of a suitable electrolyte, such as lanthanum sulphate. These were the tests exhibited:

NORMAL SERUM.

Tube.	1	2	3
Glacial acetic acid	1·0 c.c.	1·0 c.c.	1·0 c.c.
Serum	2 drops	3 drops	4 drops
Saturated solution of lanthanum sulphate in glacial acetic acid	0·2 c.c.	0·2 c.c.	0·2 c.c.
Result read twenty-four hours later	f. p.*	+	− +
SYPHILITIC SERUM.			
Result read twenty-four hours later	f. p.	(f. p.)	+

In the above tests the differences were most marked the next day. In order to read the results quickly, the following procedure was the best to adopt: To a tube containing 2·0 c.c. of glacial acetic acid add 0·5 c.c. of serum. Then obtain four test-tubes and add the following quantities of the acid serum:

NORMAL SERUM.

Tube.	1	2	3	4
Glacial acetic acid	1·0 c.c.	1·0 c.c.	1·0 c.c.	1·0 c.c.
Acid serum	2 drops	4 drops	6 drops	8 drops
Saturated solution of lanthanum sulphate in glacial acetic acid	0·2 c.c.	0·2 c.c.	0·2 c.c.	0·2 c.c.
Result in a few minutes	+	+ +	+ + +	+ + + +
Result in one hour	+	+ +	(f. p.)	(f. p.)
Result in four hours	(f. p.)	(f. p.)	(f. p.)	f. p.
SYPHILITIC SERUM.				
Result in a few minutes	(f. p.)	(f. p.)	(f. p.)	(f. p.)
Result in one hour	(f. p.)	(f. p.)	(f. p.)	f. p.
Result in four hours	(f. p.)	f. p.	f. p.	f. p.

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* f. p. = complete flocculent precipitate; (f. p.) = partial flocculent precipitate: ++++. +++. ++. +. −+ = varying degrees of opacity, water being − = perfectly clear.

The CHAIRMAN said he would be glad if anyone who had positive knowledge on this subject would help them towards its elucidation. He had ascertained the fact that these sera had been taken from patients who had not been treated in any way. As no one seemed to wish to discuss the matter, he would simply say he hoped Mr. McDonagh would go on and would continue to show them the results which he obtained, because he was sure they were all enormously interested in the subject which he had opened up so energetically.

Dr. W. KNOWSLEY SIBLEY showed a case of *Pityriasis rubra pilaris*. The boy, aged 17 years, had had the skin condition of which he complained for the last nine years. He stated that he had a bad attack of measles, and on recovering from that this rash persisted on his upper lip and the scalp, and ever since that day he had had an eruption on many parts of the body. The point arose as to whether the attack he had was measles. A year or two later he was told he had ringworm of the scalp, but there again he doubted the diagnosis. X-rays had never been applied to his scalp, but he presented a typical extensive condition of Pityriasis rubra pilaris, and he had considerable Alopecia cicatrisata, with superficial scarring on top of the scalp. There was a marked infiltration of the hair follicles on the eyebrows and the backs of the fingers, as well as on other parts of his body, especially over the arms, forearms, back, lower abdomen, and thighs. Why he should have this seborrhœic condition round the mouth he did not know.

In June, 1913, he showed a little boy, aged 9 years, who had Pityriasis rubra pilaris and Psoriasis in the opinion of most of the members who were present. He hoped to have had him up to-day for comparison. At the time he showed him he was distinctly ill, with an elevated temperature. He gave him radiant heat baths and, internally, thyroid gland. A few weeks afterwards he had become quite well. The only remaining evidence that he had ever had Pityriasis rubra pilaris was that he still had marked infiltration of the skin follicles on the fingers and over the coccygeal region. From that date he had kept comparatively well. Recently he had had signs of another Psoriasis attack, but only slight.

With regard to treatment, on the supposition that this condition was allied to Psoriasis, he had commenced to treat him with X-rays. Three weeks ago he had one-third of a pastille of X-rays applied to the right hand and forearm, repeated at the end of a week. He had now had three treatments over that region, and if they compared that region with the opposite side they would see considerable improvement; individual follicles no longer stood out on that hand, and after a few more such applications he thought the condition would clear up.

The boy whom he showed in 1913 had an extraordinary thickening of the skin of the face. The thickening subsided, but marked scars were left by the side of both eyebrows. He did not know whether scarring following this condition had been described previously.

The CHAIRMAN said it had always struck him as an extraordinary fact that a disease so characteristic in its features as Pityriasis rubra pilaris should not have been recognised by the dermatological public of this country until the year of the first Paris Congress, 1889, when several cases of it were shown. Ever since then they had all been perfectly familiar with it—that is to say, with its gross appearances. But he remembered that before 1889—about 1885—Dr. Liveing showed a case of this sort at the Dermatological Society, which he called "a peculiar psoriasis." That passed, and was supposed to be a satisfactory description. But perhaps the diagnosis was not so far amiss as one might think, because the curious relationship of this disease to Psoriasis had been fairly well established by Dr. Sibley in a previous case which they remembered, by Dr. Adamson, Dr. Graham Little, and by others in this country. The two diseases sometimes coincided, sometimes they alternated; and although the lesions of the two conditions were different in every way, there appeared to be some sort of correlation between them. In this case the seborrhœic distribution of the disease was very marked. He supposed that ultimately this boy would get quite well, as the immense majority of such cases did.

Dr. H. G. ADAMSON did not think it was by any means the general opinion that Pityriasis rubra pilaris was related to Psoriasis; his own view, which he had expressed before, was that Pityriasis rubra pilaris was in some way related to Psoriasis, since attacks of Psoriasis sometimes alternated with Pityriasis rubra pilaris in the same patient, and Dr. Little and others had recorded cases of Pityriasis rubra pilaris with Psoriasis in other members of the family.

Dr. GRAHAM LITTLE said that Dr. Adamson had referred to his case of a girl who had Pityriasis rubra pilaris for at least nine years. He saw the sister, and she had a perfectly typical Psoriasis, which had existed upon her for many years. He rather deprecated associating the two; Pityriasis rubra pilaris was an extremely rare disease. If there were any causal connection with Psoriasis, he did not see why it should not be met with more frequently than was the case. He also thought the histology was different as well as its behaviour to treatment, for he did not feel sanguine about the treatment of these cases by any of the means at his disposal. In some cases, however, the condition had disappeared spontaneously, as in one instance under his observation.

Dr. MACLEOD had observed the association of Psoriasis and Pityriasis rubra pilaris, but he did not consider that they were phases of one disease, for remedies which influenced Psoriasis had no apparent effect on Pityriasis rubra pilaris. With regard to Dr. Sibley's reference to treatment of the Pityriasis rubra pilaris by X-rays, he was not so sanguine as to the X-rays causing the Pityriasis rubra to disappear. In his experience, the X-ray treatment of Psoriasis was not always effective, for although certain patches melted away under the influence of the rays, occasionally old-standing patches did not appear to respond to them unless they were given in dangerous doses.

The CHAIRMAN said it occurred to him that a case so extensive as this might yield to light baths, as Lichen planus sometimes did.

Dr. S. E. DORE wished to ask the exhibitor if he regarded the patch of alopecia on the scalp as due to the same process which affected the skin of the body. It was well known that this disease affected the scalp, but, as far as his experience went, it did not cause cicatricial patches. The boy said he had had much discharge from the scalp, and the baldness might be due to some other process; it resembled Folliculitis decalvans very closely.

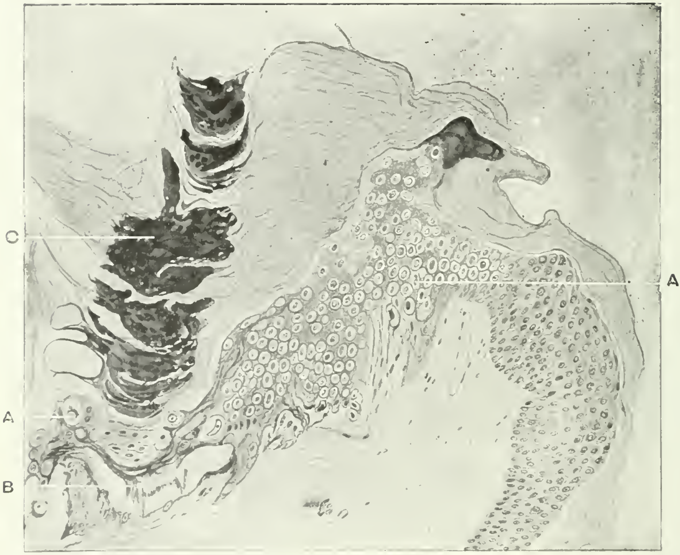
Dr. SIBLEY (in reply) regarded the condition of Alopecia cicatrisata as the result of the inflammation which had affected the hair follicles of the scalp. He was supposed to have had ringworm, but he doubted that. With regard to light baths, he treated the other case which he brought forward three years ago with electric light baths and he got well. As this boy had only had X-ray treatment three weeks, it was early yet to know what the result was likely to be. He thought it would clear up the condition in that area, and would be pleased to bring the case forward again if it was so.

Dr. E. G. GRAHAM LITTLE showed a case of *Darier's disease*. The patient was a woman, aged 28 years, sent to him by Dr. Grosart Wells, of St. Albans, who had had the case under observation for the past twenty years, and to him he was indebted for permission to bring the patient here to-day and for some excellent notes. Dr. Wells wrote: "June 14th, 1916: I have known this girl for nearly twenty years, and a skin affection of the upper lip and around the mouth dates back nearly the whole of the time. I looked upon it as an eczema, and upon her general condition as strumous, knowing she had some still earlier hip-joint disease. Her mother at the time (twenty years ago) had been in receipt of parish relief for a previous thirteen years, having fibroid phthisis. The mother is still alive. For years I did not see this girl, and until just before the date you very kindly saw her. In the interval she had attended a sea-bathing institution, and been under treatment, returning with a certificate that she was suffering from favus, and this diagnosis I passed on to you with the girl. Ointments and medicines never gave any satisfactory result in the case."

The eruption seemed to have become troublesome to the patient, more especially some twelve years ago, being notably present on the forehead, the scalp, the chin and neck. From these parts it spread slowly but persistently to occupy the areas in which it was now found:

the chest, where it was very copious and formed a fairly continuous sheet with the eruption on the neck, over the mammæ and below these, and again around the navel, and on the side of the thorax and on the suprapubic region. There were more scanty and discrete lesions scattered over the back of the trunk and on the upper part of the thighs. These lesions were very uniform in appearance, consisting of a yellowish keratosic excrescence about $\frac{1}{8}$ in. in diameter and about $\frac{1}{8}$ in. in height. Less characteristic and less frequently met with, and then mostly in parts where the eruption was scanty—as, for example, on the shoulders—were some flatter wart-like elements, resembling the "juvenile flat wart." On the dorsum of the hands there were several of these, as well as some quite typical common "cauliflower" warts, these probably being of later and accidental development. The nails were split vertically on several digits of the fingers but not on toes. They had never been shed. The skin of the palm was thickened and hyperkeratosic. The scalp was extensively affected, probably more so than any part, and the small elevations could be readily felt, on passing the hand over it, as an almost continuous sheet of eruption; but notwithstanding this involvement and long continuance, for the eruption appeared here very early, there had been no loss of hair. There was a particularly thick distribution of the characteristic papules behind the ears. The face—the chin and the temples especially—was conspicuously affected. On the chin there was a crusted seborrhœic-looking eruption disguising the underlying papular sheet, and it was probable that the affected skin readily becomes eczematous, for when she first came to his department the case was for the moment mistaken for a seborrhœic eczema, until examination of the covered parts showed the real nature of the disease.

The patient gave a history of having had an abscess of the hip-joint at the age of twelve months, which was followed by ankylosis of the left hip-joint. Probably as a result of the lack of freedom of movement in the joint there was a chronic and rather fœtid vegetative growth in the sulcus separating the thigh from the abdomen and the vulva. But there were no vegetations elsewhere, and it might be mentioned in particular that the axillæ, where these vegetations were frequently met with, were quite free, though there were numerous keratosic papules there. There was no family history of similar eruptions.



A. "Corps ronds" of Darier. B. Fissure in deeper layers of rete.
C. Plug of stratified horn-cells and débris.

DR. GRAHAM LITTLE'S CASE OF DARIER'S DISEASE.

[*To face p. 265.*

Comments.—The case reproduced with extraordinary fidelity the chief characteristics in the magistral description by Darier of his original cases. Thus the initiation of the eruption on the face and temples and scalp, the absence of loss of hair, the development of the disease at an early age, the changes in the nails, the warty lesions on the hands, which, as Darier remarked, "can in no way be distinguished from flat warts," the extraordinary resistance to treatment, the seborrhœic distribution, were all present. The colour of the lesions was perhaps unusually yellow, so much so as to allow of a diagnosis of "favus" by well-qualified medical men. The diagnosis was established by the absolutely typical appearance of the sections.

Histology.—A patch showing very characteristic lesions was excised from the abdomen. Sections were stained with Gram's stain and examined for micro-organisms, but with a negative result. Sections stained with hæmatoxylin and eosin showed a characteristic follicular hyperkeratosis, the stratum corneum being very thickened, especially about the follicles, which were plugged with scales in the affected area. The whole rete seemed rather more loosely attached to the corium than usual, and dehiscence was frequent. The changes in the epithelial cells, which led to the earlier and erroneous identification with psorosperms, were very pronounced, especially in the uppermost layers of the rete. Here there were very numerous double-contoured "corps ronds," some of enormous size. There was no resemblance to a papilloma visible in the section, although the clinical simulation of this effect was so close.

Dr. H. G. ADAMSON said on first seeing the patient he did not think it was Darier's disease. He thought the lesions were not so soft or greasy as they were in Darier's disease. He regarded them as merely multiple plane warts. She certainly had quite ordinary warts on the hands, and those on the shoulders, when viewed under the glass, closely resembled plane warts. But the microscopical section made it quite clear that the diagnosis of Darier's disease was the correct one.

The CHAIRMAN thought the microscopic evidence in favour of Darier's disease was unquestionable and decisive. The likeness of the lesions on the shoulders and hands to warts was, however, very striking. The condition appeared to him to have progressed unusually slowly if she had had it for twelve years. A few cases of the disease which he had seen, especially in France, had, he thought, been much more rapid in their course. The "Keratosis follicularis" cases of Dr. J. C. White, of Boston, were surely much acuter. They were very much indebted to Dr. Little for having brought the case; he had learnt very much by seeing it.

Dr. **MacLeod** regarded Dr. Little's case as typical of Darier's disease. He had this patient under his care at Charing Cross Hospital for three years, from 1909 to 1912, and had ample time for studying her eruption. The condition of her skin did not seem very different now to what it was then. At that time all manner of local treatments were tried, but without marked benefit. In 1904 he had the opportunity of studying a case which was under Dr. Ormerod at St. Bartholomew's Hospital, a report of which was published by Dr. Ormerod and himself in the *British Journal of Dermatology*, September, 1904. That case was very much like the one exhibited to-day, except that the lesions were slightly pigmented and the face not so markedly involved. The nature and ætiology of this rare affection remained unknown. The "corps rond" seemed to him to be due to an imperfect process of cornification of the prickle cells, which, to a slight extent, resembled that which occurred in Molluscum contagiosum, and he had wondered if this affection could not be an infective condition due to some micro-organism which found a suitable soil in certain individuals in the situations usually affected.

Dr. **Sibley** noted with interest the Chairman's observation that he had seen other cases, all of which had made more rapid progress than this. Therefore he wondered whether there was anything special in this patient's history. The patient had a hip accident followed by abscess, and he wondered whether it was tubercular, as such cases generally were; that might account for the retardation of the process. If the lesions were warty, why not try ionisation with magnesium sulphate or zinc. It could be tried on the hands first of all, and if successful its use could be extended to other parts of the body.

Dr. **Graham Little** (in reply) said that when this patient first came he was puzzled; it was a very hurried out-patient morning. He saw on her a mass of what seemed to be ordinary eczema of the face, which showed an extensive weeping condition. But he was puzzled by the history. She appeared to have had it for a very long time, and further examination revealed the condition on the body. This was the first case of Darier's disease he had had under his own care, though he had been associated with other cases, and he had no ideas about treatment. If it was infective, as suggested, one could scarcely understand a disease so long-lasting giving rise to no histories of infectivity. Hereditary transmission, but not actual infections, has been frequently noted. There was no history of inheritance in his case.

Mr. H. C. **Samuel** showed a case of *Lichen planus hypertrophicus*. The patient is a married woman, aged 65 years, with two children. The condition, for which she attended St. Bartholomew's Hospital, began eighteen years ago. Eleven years ago she was under the late Dr. Colcott Fox and Dr. Adamson. The present state was fairly typical of Lichen planus hypertrophicus, but he was not familiar with this appearance of what looked like centrifugal spread with scarring in the centre, a condition one associated with granulomata. The mucous membrane of her mouth was affected, and she confessed to the presence of another patch on her back. As usual, the condition was extremely resistant to treatment. A large variety of applications, X-rays amongst them, had been made, as usual without result. The scarring in the centre was not the result of X-rays, as the appearance had been the same before the X-rays were applied. He attempted to treat some of the spots with CO_2 snow, but the patient would not submit to this. In one case of Lichen planus hypertrophicus recently under his care he practically got rid of the lesions by firm and long exposures to CO_2 snow; this was a case which had failed to be influenced by X-rays and local chemical applications. The patient in the case he was showing said that "water comes away at times" from some of the spots, but he had never seen a vesicle or bulla when she had been under examination.

He would be grateful for suggestions as to treatment. Did the members regard the central areas as scar tissue? If so, did they agree that it was spontaneous and not the result of treatment? Ought one, in that case, to label it "atrophicus" as well, or had Lichen planus atrophicus (so-called) a different clinical meaning?

Dr. GRAHAM LITTLE said that he showed a case a year or two ago of very pronounced Lichen hypertrophicus in which he got extremely good results by shaving with a razor until the parts became sensitive, then freezing the shaved portions with snow. He thought X-rays were useless, and he had given up using them for it; he much preferred the method he had mentioned. If they only did a little at a time they could get patients to submit to it fairly readily.

Dr. S. E. DORE said that some time ago he showed there a case of hypertrophic Lichen planus as extensive as this, though the lesions were much smaller. It was suggested by more than one member who was present that it was a factitious dermatitis and not Lichen planus at all. The patient was still under his care, and he had never been able to influence the condition by treatment. There was intense itching, and she had set up deep scarring of the lesions by scratching. In this case, too, he thought the scarring may be due, in part at least, to scratching and not entirely to spontaneous atrophy.

Dr. KNOWSLEY SIBLEY said this patient had had X-rays applied to some of those lesions. He was not applying X-rays in cases of Lichen planus hypertrophicus any longer; he was reluctant to do so. A few years ago he applied the rays to a patient, and as a result she devoloped a typical patch of hypertrophic Lichen planus on the back of the hand, the lesion being of the same diameter as the diaphragm used. The condition then appeared on various parts of her body. On one occasion she burnt the back of her hand with hot water, and the seat of the bleb was followed by Lichen hypertrophicus. At one time she had extensive ulceration of the arm, and it was eighteen months before it healed up, which it eventually did under treatment with scarlet red ointment.

The CHAIRMAN thought the treatment which Dr. Graham Little had suggested was introduced into this country by Mr. Morrant Baker more than thirty years ago. He used it with success, and it is the best measure at our disposal for many of these cases. He was glad to hear a general confirmation of his own experience as to the failure of X-rays. He had never seen benefit follow X-rays and he had seen harm from them. Carbon dioxide snow had also proved disappointing in his hands.

Dr. **Alfred Eddowes** showed a case of *Dermatitis herpetiformis.* The patient, a boy, aged 5 years, for three months had had a vesicular eruption breaking out symmetrically just above the buttocks. The vesicles were always clear when they first appeared in little groups, but were soon broken by scratching, after which they sometimes suppurated. There were pitted scars to be seen. The mother told him that the child had a similar outbreak on the leg further down two years ago. During the last three months the eruption had been entirely confined to the buttock region. It was bilateral, and had very much the distribution of herpes. There was a family history of tubercle on the mother's side. The boy had a barrel-shaped chest, and he was told that the abdomen had been more prominent than it was now. He had shown great liability to catch cold, and rhonchi could be heard, though as yet there were not any signs of consolidation. He would be glad to hear any criticisms of his diagnosis.

Dr. S. E. **Dore** suggested that this child's eruption was due to the irritation of the urine on the skin. He showed, about a year ago, a case in which a boy had a similar eruption as the result of nocturnal enuresis, and he was still under his care. On giving him thyroid both the eruption and the nocturnal incontinence improved, but relapsed when the drug was stopped. This patient suffered from incontinence of urine at night, and he did not think there was sufficient evidence on which to make the diagnosis of Dermatitis herpetiformis: the eruption was localised, it had only been three months under observation, and had only been treated quite recently.

Dr. G. W. **Sequeira** suggested that this case was one of bullous impetigo. The child had one or two disk like lesions about the mouth, covered with an adherent scale. Sabouraud considered this condition due to staphylococci. He thought the bullous impetigo in this case was due to such infection.

Dr. **MacLeod** was not quite convinced of the correctness of the diagnosis of Dermatitis herpetiformis, nor was he certain that Dermatitis herpetiformis did occur in childhood. The chronic pemphigus of children, cases of which had from time to time been recorded as cases of Dermatitis herpetiformis, did not itch, nor were the lesions, as a rule, grouped in a herpetiform manner.

The **Chairman** also had some doubts as to the diagnosis of this case, as he had of any case diagnosed as Dermatitis herpetiformis in a patient aged below 12 years. There were so many possible causes of local infection that one could not eliminate them, and certainly the lesion there did not seem to be the characteristic one of Dermatitis herpetiformis as it was seen in adults. There was a general consensus of opinion that many cases put down as Dermatitis herpetiformis in young children were merely infected urticarial lesions, and such he believed to be the nature of the case exhibited.

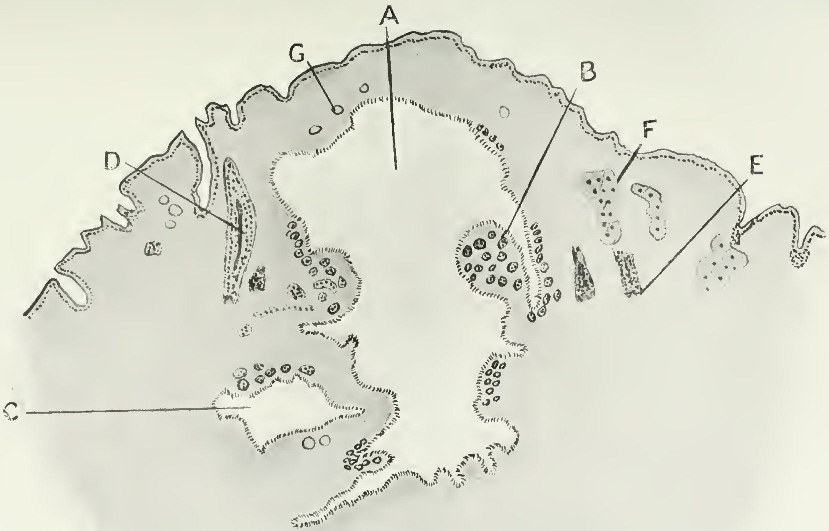
Dr. GRAHAM LITTLE was disappointed that the Chairman should lend his authority to the statement that Dermatitis herpetiformis was not to be diagnosed in a patient aged under 12 years. He thought it was very much a dispute about names, whether we call it Pemphigus or Dermatitis herpetiformis. It did not really matter if we meant the same disease. It was his experience that there was a disease which to him was definitely Dermatitis herpetiformis, and which was encountered not unfrequently under the age of 12 years. Only that morning he saw in his out-patient department two cases in children under the age of 10 years, who had been attending there for some months, two perfect specimens of what he would call Dermatitis herpetiformis—*i. e.* extremely itchy grouped bullous eruptions, persisting for long periods, controllable by arsenic, relapsing immediately when the drug was withheld.

The CHAIRMAN said that he drew a firm clinical distinction between Dermatitis herpetiformis and Pemphigus. Pemphigus in children was quite frequent, but Dermatitis herpetiformis was extremely rare in them.

Dr. EDDOWES (in reply) said he had at present in hospital a perfectly typical case of extensive Dermatitis herpetiformis, and he thought there was a wonderful similarity in the character of those patches with this. This child marked easily with scratching, and there was an urticarial element in the dermatitis. In fact, both in this case and the other he had mentioned, before the vesicles came out there were formed raised patches upon which the vesicles developed. There was no sign of pus at the beginning. One patch on the front of the abdomen in his adult case was a study. It was now becoming pigmented, just as the affected areas in the present case were. As this boy had a wheezy chest, he would be glad to give him small doses of arsenic. Might not the nocturnal enuresis go with this? Were not these patches in an area in which bladder reflexes would be manifest?

Dr. E. G. GRAHAM LITTLE showed sections from a *Papilliferous sudoriparous cyst of the cheek in a man.* The patient was a master baker, aged 54 years, under the care of Dr. S. A. Clarke, of Horley, who sent him to him on May 8th. He was a tall, thin, sallow man, much overworked, and his occupation, which entailed long hours in a hot and stuffy atmosphere, probably had some connection with the development of the tumour. This had been first noted some sixteen years ago, so that it appeared, when he was aged about 38 years, as a single, circumscribed, colourless, painless elevation, which had slowly grown larger. It was situated on the left side of the chin about halfway between the outer angle of the mouth and the ramus of the lower jaw. During the past few months it had grown somewhat faster, and a deep bluish colour on the surface had replaced the previous colourless aspect which it had maintained for many years. The surface of the skin over the tumour was and had always been intact, no discharge or scab having been noted at any time. On palpation the swelling was found to be larger than inspection of it seemed to indicate, and its base occupied an area of about $\frac{3}{4}$ in. It was deep-seated and freely movable with the skin, to which it was obviously firmly attached. It was raised about $\frac{1}{2}$ in. above the general level of the surrounding skin, and was about the size of a medium Barcelona nut, but gave the sensation of being considerably more voluminous below that level. It was moderately hard and tense to the touch except for a perceptible softening on the surface, especially on the blue part, which did not cover the whole extent of the prominence. No enlarged glands could be found in connection with it, and there was no tenderness on manipulation. The disfigurement was considerable, and the patient was readily persuaded to suffer its removal, which was effected by his colleague, Mr. Aubrey Pannett, to whom and to Dr. Kettle, Pathologist to St. Mary's Hospital, he owed his thanks for the specimen.

Sections were cut in paraffin and stained by various methods. On naked-eye inspection of the section it was obvious that the greater part of the swelling was formed by a large cyst of very irregular shape, with numerous papilliferous projections into its lumen from its walls. The general bearings were best revealed by examination with a low magnification, ocular 3, objective of a focal distance of 3 in. being used. The drawing appended was made with this magnification, by the help of a camera lucida, and the proportions and topography may thus be taken as strictly accurate. The epidermis was seen to be intact throughout; numerous sections were examined at different levels of the block, and nowhere was there any opening from the cyst communicating with the surface, from which it was, in fact, separated by a very considerable zone of felted fibrous tissue, which formed a thick capsule to it. The epidermis immediately above the cyst was thinned, the interpapillary processes flattened out, and the hair follicles and sebaceous glands mostly displaced by fibrous tissue. Beyond the margin of pressure exerted by the cyst these appendages were quite normally present. Further inspection revealed, in addition to the main large central cyst, a number of smaller cysts, one especially, situated more deeply, being about one-fifth of the size of the chief distension, and having like this numerous



A. Large cyst. B. Dilated sweat glands in papilliform projection. C. Smaller cyst.
D. Hair shaft. E. Papilla of hair. F. Sebaceous gland. G. Blood-vessels.

DR. GRAHAM LITTLE'S CASE OF PAPILLIFEROUS SUDORIPAROUS CYST.

[*To face p. 270.*

papilliferous projections from the walls. The smaller cysts were of much less size, tailing down to merely dilated sweat glands, which were very numerous, indicating a distinct hyperplasia of gland tissue. In several cases it was possible to see coil glands apparently opening on to the main cyst, but with this exception there was no break in the continuity of the containing wall of the cyst. In parts this was thinned to the dimensions of almost a single row of cells; in other parts there was a considerable thickening of the wall so that it was several layers thick. The epithelium lining the cyst was mostly columnar in shape; in the very thin parts the cells were more of a pavement shape, and in the thickened areas the cells forming the wall were in many places in actual continuity with the walls of sweat glands, some of which, as had been said, apparently discharge into the lumen of the main distension. The lumen of the two larger cysts and of some of the smaller cysts was filled with blood corpuscles, and the presence of blood doubtless explains the blue colour of the tumour in its later growth. The vessels throughout the section seemed rather thin-walled, but not otherwise altered. There was no resemblance to a hæmangioma.

Comments: This type of growth would seem to be infinitely rare, for the only instance quite certainly comparable in his opinion with his case was the single case reported by Rolleston.* This tumour also occurred upon the face, was not congenital, appearing for the first time when the patient was aged 17 years, and the same curious papilliform projections from its wall into its lumen were a conspicuous feature. Rolleston regarded his case as of the same nature as two reported earlier, one by Robinson and one by Elliott. Robinson's case was apparently not congenital, for it was stated that the growth had been noticed only a short time, the patient being a girl, aged 13 years. There was no mention made of sweat-glands being in any way abnormal; and beyond the statement that the contents of the cyst were a clear non-sebaceous fluid, which was not analysed, there was no very convincing evidence of its connection with the sweat apparatus. The tumour was in the axilla, and the argument was used that in that situation sweat-glands are especially active. Histologically the papilliform projections into the lumen from the lining wall of the cyst were especially remarked. There was a remarkable case reported by Thimm, in which very numerous tumours (as many as 150 being ultimately counted) made their appearance on the skin of a youth at the age of 17 years, chiefly over the sternum, but also on the neck, axillæ, and elbows. This perhaps may be classed with Robinson's, Rolleston's, and his cases respectively. Sections from one of these nodules showed a large cyst in the corium at the level of the sweat-coils, which were greatly hypertrophied and distended. The case reported by Dr. Adamson on behalf of Dr. Norman Paul, of Sydney, in the *British Journal of Dermatology*,* was apparently also of this nature, and the lesions similar in position. The patient was a man in whom the first development of tumours had taken place at the age of 19 years, over the lower end of the sternum, and in whom, as in his case, the growth later assumed a blue colour, which was demonstrated histologically to be due to extravasation of blood into the dilated cysts. Some other cases, which were regarded by some authorities as of the same nature, were sharply differentiated by the fact that the cysts which had been described (on doubtful data, as it seemed to him) as connected with sweat structures occurred in tumours which in other respects, and especially in their congenital origin, were undoubtedly to be classed with the nævi. Petersen's case. Elliott's case, and four cases described by Walters as Nævi syringo-adenomatosi were of this type; in all these the histological features include more or less solid downgrowths of epithelium from the epidermis into the corium, after the manner of nævi, of the type of moles. To his mind this fact offered a very convincing differentiation from the case reported, in which the epithelial hyperplasia was deeper in situation and found chiefly at the level of the sweat-coils, being, indeed, conspicuously absent in the zone immediately below the epidermis.

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* *Brit. Journ. Derm.*, 1904, xiv, p. 83.

Dr. H. G. ADAMSON remarked that at a recent meeting of this Section, as stated by Dr. Graham Little, he showed sections of a case for Dr. Norman Paul, of Sydney, in which the lesions were clinically very like those of Dr. Little's case. The microscopical appearances were, however, not so frankly those of sweat-gland tubules, but those of a more embryonic, less differentiated "syringoma," and such as are found in cases of multiple syringomata or "Lymphangoma tuberosum multiplex." Notes of Dr. Paul's case were published in the *British Journal of Dermatology* for June, 1916.

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* *Brit. Journ. Derm.*, 1916, xxviii, p. 106.

CURRENT LITERATURE.

INFLAMMATORY AFFECTIONS.

DE L'ÉRYTHÈME ANNULAIRE CENTRIFUGE (ÉRYTHÈME PAPULO-CIRCINÉ MIGRATEUR ET CHRONIQUE) ET DE QUELQUES ÉRUPTIONS ANALOGUES. J. DARIER. (*Ann. de Derm. et de Syph.*, 1916–17, vi, No. 2, March, 1916, p. 57.)

DARIER describes a case which he observed many years ago, and which he believes to be related to, but yet distinct from, Erythema polymorphicum of Hebra, and to merit a special name.

The patient, L—, aged 26 years, an artist, first came under observation in 1898, with an eruption which had been regarded as syphilitic. The eruption consisted of circles and rings abundant on the lumbar region, the buttocks, and the posterior surface of the thighs, less profuse on the lateral parts of the back, the anterior surface of the thighs, and the forearms. Each lesion began as a rose-coloured papule ½ to 1 cm. in diameter, flat, or depressed at its centre, and firm to the touch. Soon the border extended excentrically into the form of a vivid rose ring 4–6 mm. in diameter and raised 2–3 mm., feeling like a hard cord. In a week the ring reached the size of a franc or even that of a five-franc piece. Some rapidly disappeared, leaving a pigmented macule; others met neighbouring rings and formed festooned patterns, which reached the size of the palm, or larger, and lasted several months. Fresh lesions continued to appear for nine months, and then the whole eruption went, and did not return. The outer margin of the rings was abrupt, the inner more sloping towards a central area slightly pigmented, but otherwise normal. The ringed margin was continuous and not broken up into a chaplet of papules: there was neither desquamation nor vesication, and there was no pruritus.

In discussing the diagnosis from Granuloma annulare, Darier says that this eruption has absolutely nothing in common with his case.

There are only two other published cases which he considers to belong to the same class, viz. "A case of Erythema exsudativum perstans" (Otto Sachs, *Verhandlungen den Deutschen Dermatol. Gesellschaft*, vii Congr. Breslau, 1901), and "A rare form of erythema: Erythema chronicum migrans" (B. Lipschutz, *Arch. f. Derm. u. Syph.*, 1913, t. 118, p. 349). Colcott Fox's cases of "persisting gyrate erythema in the two elder members of one family—Erythema gyratus perstans" (*International Atlas of Rare Skin Diseases*, fasc. v, 1891), differ in that there was desquamation, pruritus, wider generalisation, longer duration (fifteen years), family character, and above all, in that in one of Fox's cases there was vesication during the course of one outbreak of the eruption. H. G. A.

PSORIASIS AS A SEQUEL TO ACUTE INFLAMMATIONS OF THE TONSILS. J. M. WINFIELD. (*Journ. Cut. Dis.*, 1916, xxxiv, p. 441.)

SIX cases are here recorded in which attacks of psoriasis followed some inflammation of the tonsils. In four of the cases an attack of follicular tonsillitis preceded an eruption of psoriasis, in one the skin disease followed enucleation of the tonsils, while in another it was the sequel of a streptococcic sore throat. Bacteriological examinations were made of the follicular contents and other secretions from the throat, but these did not throw any light on the cause of the psoriasis. No special organism was found in all the cases, and the writer considers that the tonsillar inflammation and the high temperatures sufficiently disturbed the metabolic balance to produce the disease in one predisposed to it. J. M. H. M.

TREFOIL DERMATITIS: OR THE SENSITISATION OF UNPIGMENTED SKIN TO THE SUN'S RAYS BY INGESTION OF TREFOIL. SYDNEY DODD, Lecturer in Veterinary Pathology and Bacteriology, University of Sydney, N.S.W. (*Journ. of Comparative Pathology and Therapeutics*, March, 1916, xxix, Pt. I, p. 47.)

THERE occurs in certain districts in New South Wales a complaint which affects domestic herbivora, and which goes by the name of "Aphis disease." It prevails in the spring, *i.e.* in August, September, and October, and particularly after the shearing. In sheep it attacks the ears and nose, and the back particularly. There is a more or less severe inflammation of the skin of these parts, with exudation and pruritus. The skin becomes red and swollen, and the exudation forms crusts, while the scratching and biting induced by the pruritus lead to raw areas and sometimes to secondary suppuration or ulceration. It is remarkable that only the unpigmented skin is affected and those parts which are denuded of wool. In horses and cattle, too, only the unpigmented areas are involved, and animals with white or pink skins. In cows the udder and teats may be affected By stock-owners this complaint is called "aphis-disease" because they are firmly convinced that it is due to aphides, since it occurs when trefoil is green and abundant, and because trefoil is a favourite haunt of aphides. It is true that the disease is seen only in trefoil paddocks and when trefoil is green and luxuriant, and that it disappears in October, when the hot sun dries up the trefoil. But Prof. Dodd offers a different explanation of the facts. He has carried out a series of (A) experiments of feeding guinea-pigs upon trefoil and exposing them to the sun's rays; and has controlled these experiments by (B) feeding guinea-pigs on trefoil and protecting them from the sun, and by (C) feeding on ordinary diet and exposing to the sun. In experiments (A) guinea-pigs fed upon an exclusive diet of trefoil and exposed to direct sunlight developed, only upon areas unpigmented and uncovered by hair, erythema and inflammatory œdema of the skin with exudation and with pruritus. These symptoms appeared six days after the feeding and exposure began, so that the consumption of a relatively large amount of trefoil seemed essential. The symptoms disappeared a few days after stopping the trefoil as fodder. In experiments (B) no reactions took place, nor in experiments (C).

Dodd recalls other animal diseases in which there is evidence that the ingestion of a plant sensitises the skin to the action of the sun's rays. Such are: Fagopyrismus, a dermatitis due to sensitisation by buckwheat (*Polygonum fagopyrum* and *P. persicaria*). It has been found that an alcoholic extract of these plants is fatal to sun-exposed mice.

Clover disease occurs in Europe after feeding on Swedish clover (*Trifolium hyfridium*) and red clover (*T. pratense*).

The substance in trefoil which causes "sensibilisation" to light has not been determined, but Dodd refers to a paper by T. B. Rogers in the *American Veterinary Review*, No. 2, vol. xlvi, "On the Action of St. John's Wort as a Sensitising Agent for Unpigmented Skin," in which mention is made of a definite fluorescent substance which has been isolated from the plant (*Hypericum*), and which is regarded as the sensitising agent. H. G. A.

[Although this paper deals with a skin affection of animals, it is of interest to students of human dermatology, especially in regard to the suggested photodynamic action of certain fluorescent bodies in the production of eruptions such as Hydroa æstivale, and it may be useful to recall some of the previous work in this direction.

(1) "Hydroa æstivale in two brothers, complicated with the presence of hæmatoporphyrin in the urine." McCall Anderson (*Brit. Journ. Derm.*, 1898, x, p. 1).

(2) "Demonstration of the evil influences of various fluorescent bodies on infusoria exposed to light." Iodltbauer and Busk (*Arch. Internat. de Pharmac. et de Therap.*, 1905, xv, p. 263).

(3) Tappeiner "On the influence of fluorescing bodies on infusoria" (*Munch. Med. Wochenschr.*, 1900, No. 1, p. 5, 1901, p. 1810, 1903, p. 2042) found that certain fluorescent substances, such as resin, fluorescin, acridin, which were more or less inert in the dark, became poisonous in the light, and that eosin injected under the skin, and then exposed to light, causes acute necrosis.

(4) Hausmann records some experiments with white mice which became sensitised to light by injection of hæmatoporphyrin (*Wiener Klin. Wochenschr.*, 1909, No. 52, p. 1820). Hæmatoporphyrin is a fluorescent body.

(5) Ehrmann suggested that hæmatoporphyrin is the sensibilising agent in human Hydroa æstivale (*Archiv. f. Derm. u. Syph.*, 1909, xcvii, p. 83).

(6) Perutz fed animals on sulphonal (a drug which may give rise to hæmatoporphyrinuria), and thus sensitised them to light (*Wiener Klin. Wochenschr.*, 1910, xxiii, No. 4).

(7) In 1912 Perutz published experiments with other fluorescent bodies (eosin, quinine, etc.), and demonstrated that eosin enhances the light sensibilising effect of hæmatoporphyrin, while quinine is antagonistic.

(8) Pfeiffer (*Wiener Klin. Wochenschr.*, 1911). Photodynamic influence of fluorescing substances.

(9) Lewin. "The photodynamic influence of fluorescent bodies in coal-tar" (*Munch. med. Wochenschr.*, 1913, lx, No. 28, p. 1529). An attempt to demonstrate that certain eruptions which occur on the face and arms of workers in coal-tar products are the result of the light sensibilising action of alcohol soluble fluorescent bodies contained in coal-tar.

The observations and experiments noted above would seem to suggest that hæmatoporphyrin is the sensitising agent in cases of Hydroa æstivale. But in two well-defined examples of Hydroa æstivale under the writer's care repeated examinations, chemical and spectroscopical, of the blood and urine failed to demonstrate even a trace of hæmatoporphyrin. Quinine, administered to these patients according to the suggestion of Perutz, failed to diminish the susceptibility to light. H. G. A.]

NEW GROWTHS.

TWO CASES OF IDIOPATHIC HÆMORRHAGIC SARCOMA (Kaposi).

T. Caspar Gilchrist and Lloyd W. Ketron. (*Journ. Cut. Dis.*, 1916. xxxiv. p. 429.)

In this contribution two cases of Kaposi's disease are recorded. Case 1 was of the usual type, and occurred in a man aged 65 years, who presented about four or five hundred nodules, scattered chiefly over both upper and lower extremities, and a few reddish patches on the nose, cheeks, chin, and ears. The lesions varied in size from small papules or nodules up to large confluent areas several inches in diameter. The hands, forearms, legs, and feet were markedly œdematous. The treatment adopted consisted of daily intra-muscular injections of ¾ gr. of cacodylate of sodium, gradually increased to 2 gr. after ten days. The hands, legs, and feet were exposed daily to soft X-rays, and radium was applied to the nodules *seriatim*. Great benefit was derived from this treatment, and the skin lesions were improved 75 per cent.

Case 2 was that of a man, aged 58 years, who presented six distinct lesions on the face, consisting of dark red, slightly raised, deeply infiltrated patches about the size of the finger-nail. These were treated with filtered X-rays and entirely disappeared.

From case 1 an autogenous vaccine was prepared, but no definite results were obtained from its use.

The conclusion arrived at by the writers with regard to the histopathology is that "the lesions begin in the skin as angiomata, due to a proliferation and dilatation of the blood capillaries, which are very frail at first and liable to rupture. This is followed by a proliferation of the interstitial connective tissue and endothelium, which gradually obliterates the blood spaces, forming solid tumours. In the early stages these resemble, in some areas, young connective tissue, in other areas sarcomata. As the lesions grow older they assume a more fibrous aspect, and may undergo involution. Coexistent with the formation of the tumours there is a sclerosis of the small arteries supplying them, causing a gradual decrease in the amount of blood. To this is due, most likely, their later evolution as well as involution."

The disease seemed to spread by metastases, which first appeared in the neighbourhood of the primary lesion, and later became widespread both in the skin and internal organs.

J. M. H. M.

SYPHILIS.

AN EXPERIENCE OF GALYL AT ROYAL NAVAL HOSPITAL, CHATHAM.

Sheldon F. Dudley, M B. (*Lancet*, July 8th, 1916, p. 59).

At the Royal Naval Hospital galyl has been substituted for neo-salvarsan in the treatment of syphilis, and the writer compares the action and results of the two drugs. Galyl 0·4 grm. and neo-salvarsan 0·9 grm. were used, and cases were given three intravenous injections of galyl at monthly intervals with three intramuscular injections of 1 gr. of mercury after each dose of the arsenical preparation. A comparison of the three commonest symptoms of reaction, viz. rise of temperature, headache, and vomiting, based on 583 injections of galyl and 150 of neo-salvarsan, was made. Thirty per cent. of neo-salvarsan cases may be expected to develop a temperature between 100°-101° F., whereas a similar rise of temperature is only to be expected in 15·6 per cent. of galyl cases. In the same cases 18 per cent. of those treated with galyl complained of headache, while 39·3 per cent. of those treated with neo-salvarsan complained of the same thing. Vomiting followed in 3·9 per cent. of galyl injections and in 21·3 per cent. where neo-salvarsan was injected. About half the galyl cases were followed by no rise of temperature as marked on a four-hourly chart, whereas only a quarter of the neo-salvarsan cases escaped without any rise of temperature. The lesser toxicity of galyl is also very evident from the few injections that are followed by headache and vomiting, as compared with those treated with neo-salvarsan. In the author's experience reactions after second and third injections of either drug are far less common than after the first Vomiting and headache are exceptional after injections subsequent to the first. That these common febrile reactions are probably caused by the liberation of endotoxins of the *Treponema pallidum* is shown by the fact that they are less frequent after the first dose, and by the comparative freedom from reaction in late syphilitic cases. Taking the results as a whole, neo-salvarsan seems to have slightly more power in producing a negative Wassermann reaction than galyl, and a notable point is the difficulty of obtaining a negative reaction in the late stages of the disease. An attempt was made to compare the action of the drugs on the treponemata in the sores. Twelve cases in whose sores treponemata were easily demonstrated were given an injection of galyl and an equal number were given salvarsan, the lesions being examined for treponemata six to eight and a half hours after injection. Spirochætes were present in eight of the galyl as against five of the neo-salvarsan cases. No spirochæetes could be found in any of the twenty-four sores the morning following injection. In two cases treated with an intravenous injection of 1 grm. ferrivine, *Treponemata pallida* were easily demonstrated four days after injection. Clinically, galyl seems to be almost as valuable as neo-salvarsan; the dose, 0·4 grm. galyl, contains just half as much arsenic as 0·9 grm. of neo-salvarsan, which probably accounts for the slightly less therapeutic effect and lesser toxicity of the former drug. The writer suggests that the lesser toxicity of galyl is due to the fact that it has four benzene rings to the molecule: inorganic arsenic being very toxic, and having no ring; one-ringed compounds like atoxyl being less toxic, and those with two rings as "606" and "914" still less toxic. Although excellent results have been obtained with neo-salvarsan and mercury with a month's interval between the intravenous injections, this interval is unnecessarily long in the case of galyl. As the dose recommended has only half the arsenic content of neo-salvarsan, the interval could be halved without the occurrence of cumulative arsenical poisoning, and if this were done the author is of the opinion that galyl would be as successful in the treatment of syphilis as neo-salvarsan.

S. E. D.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

ERYTHEMAS, INFLAMMATIONS, ETC.

Dermatitis due to Hair-Dyes. J. L. BUNCH. (*Practitioner*, August, 1916, p. 173.)

Granuloma Pyogenicum affecting the Eyelid, A Case of. CASSIUS D. WESTCOTT. (*Journ. Amer. Med. Assoc.*, June 24th, 1916, lxvi, No. 26, p. 2067.)

Lichen Planus, Diffuse Pigmentation of the Scrotum in. D. W. MONTGOMERY. (*Journ. of Cut. Dis.*, July, 1916, xxxiv, p. 499.)

Pellagra, A Critical Study. JOHN AULDE. (*Med. Record*, July 29th, 1916, p. 181.)

Pityriasis Lichenoides Chronica, A Clinical and Microscopical Study of a Case mistaken for Lichen Planus. F. WISE. (*Journ. Amer. Med. Assoc.*, July 18th, 1916, lxvii, p. 159.)

Porokeratosis, A Peculiar Form of (photographs). S. MATSUMOTO. (*Journ. of Cut. Dis.*, July, 1916, xxxiv, p. 489.)

Psoriasis as a Sequel to Acute Inflammation of the Tonsils. J. MACFARLANE WINFIELD. (*Journ. of Cut. Dis.*, June, 1916, xxxiv, p. 141.)

Psoriasis, The Pathogenesis of. ABNER H. COOK. (*New York Med. Journ.*, August 5th, 1916, p. 255.)

NEW GROWTHS.

Condyloma Acuminatum of the Anal Region in the Male. A. RAVOGLI. (*Journ. Amer. Med. Assoc.*, July 8th, 1916, lxvii, p. 109.)

Hair-Matrix Carcinoma. FRANK WARNER. (*Med. Record*, July 15th, 1916, p. 98.)

Idiopathic Hæmorrhagic Sarcoma (Kaposi), One presenting unusual features, with special methods of treatment and investigation, Case of. T. C. GILCHRIST and LLOYD W. KETRON. (*Journ. of Cut. Dis.*, June, 1916, xxxiv, p. 429.)

Verrucæ Planæ Juveniles complicated with Lichen Planus. An Instance of. G. D. CULVER. (*Journ. of Cut. Dis.*, July, 1916, xxxiv, p. 502.)

DISEASES OF HAIR AND NAILS, PIGMENTATION, ETC.

Monilethrix, A Clinical and Histological Study, with a Report of Six Cases and a Review of the Literature. G. M. MACKEE. (*Journ. of Cut. Dis.*, June and July, 1916, xxxiv, pp. 444 and 506.)

FUNGUS INFECTIONS.

Lichenoid Trichophytides, On the so-called Secondary. M. B. PEDERSEN. (*Hospitalstidende*, 1916, No. 20.)

Microsporon Ringworm of the Scalp due to Microsporon Lanosum. G. VERROTTI. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1916, vol. lvii, fasc. ii, p. 84.)

TREATMENT.

Autoserum Injections in Skin-Diseases, The Value of. WM. S. GOTTHEIL. (*New York Med. Journ.*, June 24th, 1916, p. 1209.)

Cases illustrating the Faulty Treatment of Superficial Malignancy. H. H. HAZEN. (*Journ. Amer. Med. Assoc.*, June 10th, 1916, lxvi, No. 24, p. 1829.)

Vaccine Therapy and other Treatment in Acne Vulgaris and Furunculosis. HAROLD H. FOX. (*Journ. Amer. Med. Assoc.*, June 24th, 1916, lxvi, No. 26, p. 2064.)

RADIOTHERAPY.

Gamma-Rays of Radium on Deep-seated Inoperable Cancers of the Pelvis, The Action of. HENRY SCHMITZ. (*Med. Record*, July, 15th, 1916, p. 100.)

Radium. SINCLAIR TOUSEY. (*New York Med. Journ.*, July 8th, 1916, p. 56.)

Radium Efficiency in Non-malignant Surgical Conditions. ROBERT ABBE. (*Med. Record*, July 8th, 1916, p. 47)

Roentgen Rays, The Treatment of Tuberculous Adenitis by. RUSSELL H. BOGGS. (*New York Med. Journ.*, May 27th, 1916, p. 1016.)

PATHOLOGY.

Animal Experiments upon the Acquirement of Active Immunity by Treatment with Von Ruch's Vaccine against Tuberculosis. FRANK J. CLEMENGER and F. C. MARTLEY. (*Med. Record*, July 22nd, 1916, p. 135.)

Cutaneous Reaction from Proteins in Eczema. K. D. BLACKFAN. (*Amer. Journ. Dis. Child.*, June 1916, p. 441.)

Eczema and Protein Hypersensitiveness. Editorial. (*Journ. Amer. Med. Assoc.*, July 15th, 1916, lxvii, p. 207.)

Histopathology. The Lichens : Lichen Planus (illustrated). W. J. HEIMANN. (*Journ. of Cut. Dis.*, July, 1916, xxxiv, p. 528.)

Importance of Immunity, Allergy and the Tuberculin Reaction for Dermatology. W. L. L. CAROL. (*Nederlandsch Tijdschrift voor Geneeskunde*, Amsterdam, April 22nd, 1916, No. 17. Short abstract, *Journ. Amer. Med. Assoc.*, June 17th, 1916, p. 2044.)

Preparation of Skin-Tissue for Microscopical Study. NATHAN FREEMAN. (*Journ. of Cut. Dis.*, July, 1916, xxxiv, p. 541.)

The Microscope in Dermatology. OSCAR L. LEVIN. (*New York Med. Journ.*, July 15th, 1916, p. 117.)

Vaccinia, Variola, and Varicella, Cultivation of the Organisms of. HORACE GREELY. (*Med. Record*, August 12th, 1916, p. 265.)

SYPHILIS.

Apparatus for Intravenous Salvarsan Injection. L. R. KAUFMAN. (*New York Med. Journ.*, June 10th, 1916, p. 1127.)

Cerebral Syphilis, Early Death from, with successful Rabbit Inoculation. MATHEW A. REASONER. (*Journ. Amer. Med. Assoc.*, June 17th, 1916, lxvi, No. 25, p. 1917.)

Combined Arsenic-Mercury Treatment of Syphilis. FAVRE and LONGIN. (*La Presse Médicale*, May 8th, 1916, xxiv, No. 26.)

Congenital Syphilis. FRED WISE. (*New York Med. Journ.*, August 12th, 1916 p. 293.)

Congenital Syphilis. J. P. JONES. (*New York Med. Journ.*, July 1st, 1916, p. 11.)

Congenital Syphilis and its Modern Diagnosis, The Present Conception of. ADOLPH ROSTENBERG. (*Med. Record*, July 1st, 1916, p. 14.)

Early Syphilis. OSCAR L. LEVIN. (*New York Med. Journ.*, July 29th, 1916, p. 212.)

Ferrivine and Intramine on Syphilis, The Effect of. L. W. HARRISON and C. H. MILLS. (*Lancet*, June 17th, 1916, p. 1214.)

Galyl at Royal Naval Hospital, Chatham, An Experience of. SHELDON F. DUDLEY. (*Lancet*, July 8th, 1916, p. 59.)

Palpebral Chancre, A Case of. H. J. McGRIGOR and DONALD M. LIVINGSTON. (*Lancet*, May 20th, 1916.)

Salvarsan, A simplified method of administering. F. R. BRAYTON. (*Journ. Amer. Med. Assoc.*, June 17th, 1916, lxvi. No. 25, p. 1921.)

Wassermann Reaction. B. LEMCHEN. (*Med. Record*, July 15th, 1916, p. 107.)

Wassermann Reaction, On Dungern's Simplification of. E. RESPIGHI. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1916, vol. lvii. fasc. ii. p. 79.)

BOOKS RECEIVED.

The Treatment of Diseases of the Skin. (2nd Edition.) By W. KNOWSLEY SIBLEY, M.D., M.R.C.P. London: EDWARD ARNOLD. Price 6*s.* net.

An Introduction to Dermatology. (6th Edition.) By NORMAN WALKER, M.D., F.R.C.P. Sixty-three coloured plates, and 89 illustrations. Edinburgh and London: WILLIAM GREEN & SON, LTD. Price 15*s.* net.

When to Advise Operation in General Practice. By A. RENDLE SHORT, M.D., F.R.C.S. Bristol: JOHN WRIGHT & SONS, LTD. Price 5*s.* net.

DEATHS.

ELIE METCHNIKOFF, Sub-Director of the Pasteur Institute, Paris.

ALBERT NEISSER, Professor of Dermatology in the University of Breslau.

ALFRED WOLFF, Professor of Dermatology in the University of Strassburg.

PAUL HASLUND, First Assistant in the Finsen Institute at Copenhagen.

GUISEPPE CIUFFO, Docent in Dermatology in the University of Pavia.

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LIVEDO RETICULARIS.

By H. G. ADAMSON, M.D.

Livedo reticularis, or marbling of the skin, is a familiar appearance in many children and young adults when they are undressed and exposed to the cold.

Probably because it is regarded as but little, if at all, removed from a normal condition, it does not receive much attention in medical text-books. But it is not without interest. In the first place it is a curious fact, of which there is no satisfactory explanation, that many persons in apparently normal health present this mottling of the skin, while the great majority of healthy persons show no trace of it. It has been suggested that a marked and persistent degree of livedo may depend upon a departure from health due to tuberculosis, syphilis, thyroid insufficiency, cardiac disease, or other internal trouble; and some there are who believe that a slighter degree of livedo indicates a tendency to one or other of these complaints.

Apart from such examples of unusually marked and persistent Livedo reticularis there have been recorded a number of cases in which there is a definite inflammatory "eruption" which has taken the form of an irregular network corresponding to the network of livedo, and to which the term "inflammatory livedo" may be appropriately applied.

And, finally, a further point of interest is the circumstance that Livedo reticularis serves as a graphic representation of the distribution of the blood supply of the skin, and thus, as will be presently shown, helps to explain the manner of distribution of some of the commoner skin eruptions.

I propose to deal with each of these points in turn, after firs discussing what is known of the anatomy of livedo.

I. The Anatomy of Livedo.

The term livedo seems first to have been used by Kaposi to distinguish local or limited blue colorations of the skin from cyanosis or universal colorations. He gave the name "Livedo calorica" to the "bluish-red mottling of the skin produced by the influence of cold in some people, particularly in young subjects and in the female sex." He says that with "persons whose skin is thus sensitive to cold, if they undress in a room at a temperature of 63°–68° F., and still more if they remain for some time exposed to such temperature in a state of partial or complete nudity, their veins become injected to so great a degree that the plexures which there form can be seen exactly as on the skin of a corpse (the so-called 'post-mortem mottling'). Under such circumstances, the surface presents bluish-red or dark blue lines, of about 2 cm. in width, communicating, and forming circles or various serpentine figures. These appearances are observed chiefly on the skin of the extremities and to a less extent on that of the trunk."

Livedo reticularis is perhaps rather more often seen among out-patients at a hospital than in private practice, and the late Dr. Colcott Fox called the writer's attention to its frequent occurrence among the children in the Metropolitan Asylums Board Ringworm Schools, generally in association with cold and blue extremities, in spite of these children being well nourished and apparently otherwise healthy.

Kaposi was no doubt incorrect when he attributed the "marbling" to the injected *veins,* for the livedo network does not correspond to the superficial veins which may be often observed as bluish streaks upon the surface of the skin, but rather to areas of comparatively poor capillary circulation; and the correct explanation is, probably, that of Renaut, to which Bonnet has called attention in a recent article on livedo in *La Presse médicale.*

Renaut, in 1883, in the *Dictionnaire Encyclopédique des Sciences médicales,* described a method of injection of Prussian Blue, which he employed to demonstrate the arrangement of the vessels of the skin.

At first the injection produced rounded blue patches separated by pale tracts. The pale tracts became coloured on continuing the injection. Each of the little areas corresponding to the blue patches represents, he says, the base of a vascular cone which is fed by a deep artery at its apex. These round areas Renaut styled areas of "maximum circulation," and the intermediate tracts were "regions of reduced circulation." It follows, he says, from this anatomical arrangement that active hyperæmia will cause flushing of the areas of maximum circulation and so red patches, and that a venous stasis will produce a dusky network (Livedo reticularis) corresponding to the areas of reduced circulation.

Unna, in his *Histopathology of the Skin,* also refers to vascular cones which form round or oval segments on the surface of the skin, between which there are areas of capillary vessels which are nourished only indirectly through collateral capillaries. The central rounded or oval segments he calls "plane elements" and the reticular residue between he names the "collateral net." A congestive hyperæmia produces a roseola in the plane element. A stagnatory hyperæmia or cyanosis produces a grey-blue coloration of the collateral net, *i. e.* Livedo annularis. He regards Livedo annularis a frigore as half-way between the general anæmia of the skin produced by extreme cold and the simple diffuse cyanosis of cold. In livedo the vessels of the central plane areas are contracted, while the circulation in the collateral net is delayed.

While dealing with the anatomical side of Livedo annularis it is interesting to recall that Auspitz, in 1874, in his classical article, "Ueber venöse Stauung in der Haut," gave an account of some experimental researches on the results of prolonged constriction of the forearm by a venesection band, and published several coloured plates which depict the exaggerated reticular network so produced in the arm of a healthy person, and also the effect upon the eruption in cases of measles and small-pox.

II. PERSISTENT AND PRONOUNCED LIVEDO ANNULARIS ASSOCIATED WITH VARIOUS ILLNESSES.

Livedo annularis may sometimes be present in an exaggerated and persistent form in association with cold and blue extremities, and in

France especially, the question has been raised as to whether in such cases livedo is to be regarded as a pathological condition indicating tuberculosis or a tuberculous tendency or some other departure from health. In 1911–13 several papers and reports of cases appeared dealing with Livedo annularis, particularly in children, by Comby, Jourdanet, and Lucas-Championnière; and Guille, a pupil of Comby, wrote a *Paris Thesis* on livedo. Comby, in his paper, illustrated by some striking pictures of livedo in children, says that one may see livedo in congenital syphilitic infants, in the myxœdematous, in Mongolian idiots, among scrofulous and tuberculous children and among rachitics, and that children with livedo often react to tuberculin and are frequently of tuberculous parentage. Guille reports twenty-one cases in children and adults, and concludes that persistent livedo may be symptomatic of a more or less disturbed general condition, such as is the case in a varicose, rheumatic, hypothyroideal, or tuberculous state. He suggests that these various affections may exercise an action upon the sympathetic nerve plexus in certain predisposed persons by the production of toxins; but an unusual case of livedo which I have recently had under observation leads me to think that pronounced and persistent marbling is not so readily explained as a physiological disturbance, and that there may be some local anatomical departure from the normal. In the case to which I refer there was a segmental distribution of the livedo, parts of the body having a normal skin without any marbling, while other large areas showed a definite Livedo reticularis (Fig. 1). The patient was a lad who had unilateral hypertrophy of the face associated with livedo of the greater area of the skin, but with one half of the chest and back without a trace of marbling.

III. Reticulated Livedo-like Eruptions or Inflammatory Livedo.

Apart from such instances of pronounced or persistent generalised Livedo annularis, which may be regarded as exaggeration of a normal condition, others have been recorded from time to time in which there were more or less limited areas of congestive mottling up to a definite inflammatory condition, often with pigmentation, which followed the lines of Livedo annularis.

Among these cases we may include the well-known Erythema ab igne or Ephelis ab igne, and other, somewhat rarer, cases associated with various visceral troubles or pathological states, such as rheumatism, tuberculosis, syphilis, hepatic and nervous diseases. Only a brief reference need be made to the better known Erythema ab igne, but the few published cases of the rarer condition will be dealt with more fully.

(a) *Erythema ab igne and Ephelis ab igne.*

The best known forms of livedo-like eruption are the localised exaggerations of this marbling which occur as the result of continued exposure to heat, as on the knees, thighs, and legs of persons who habitually sit over the fire, who work at a furnace, or who, as in France, employ a chaufferette. In these cases congestion is followed by chronic inflammatory thickening, and even vesication and considerable pigmentation is produced. Examples of such cases have been recorded by Perry, Crocker, Pringle, Sequeira, Hartzell, myself, and others, and the photograph here published represents a good example of this condition (Fig. 2).

(b) *Examples of Livedo-like Eruptions associated with Rheumatism, Visceral Troubles, Nervous Troubles, and with Tuberculosis.*

Apart from this well-known Erythema ab igne, there are in dermatological literature a limited number of cases of what may be called "inflammatory livedo"—that is to say, of a reticulated eruption in which the network follows the lines of Livedo annularis.

(1) In 1883 Cavafy described in the *Clinical Society's Transactions* two cases of "symmetrical congestive mottling," and his paper is illustrated by reproductions of water-colour drawings. Both patients were single women, aged 22 and 21 years.

Cavafy described the mottling as an exaggeration of the marbling often seen on the skins of children and young persons after exposure to cold (Livor e frigore), though less uniformly distributed. The congestion remained more or less evident at all times, though intensified by cold, and was more strongly marked than in Livor e frigore, and was followed by pigmentation. It occurred above and below the knees and on both arms and wrists and hands with symmetrical distribution. Cavafy thought it probably due to a vasomotor neurosis allied to the local asphxia of Raynaud. One of the cases had a form of rheumatism with shifting effusions of joints, and with Raynaud-like attacks in the fingers.

Cavafy also mentions the case of a man who had heart disease and old embolic right hemiplegia in whom the skin was œdematous, cold, and marbled, especially about the elbow and leg of the paralysed side.

(2) Crocker, in *Diseases of the Skin*, 3rd edition, p. 71, under the name "Congestive Mottling in Rings," refers to the case of a child under Dr. Barlow in whom, when the legs were exposed, purplish rings, about an inch in diameter, with clear centres, appeared slowly on the thighs, and another instance in a man with locomotor ataxy shown by Dr. Lees at the Dermatological Society.

(3) Ten years after Cavafy's case Unna published a remarkable case, which he called "Asphyxia reticularis multiplex." It was published in the *International Atlas of Skin Diseases* (1893) with a coloured drawing. It appears to be a unique case, unless it can be put into the group of papulo-necrotic tuberculides, as perhaps some of the cases which I shall presently mention suggest. The patient was a woman, aged 40 years, strong and well nourished, who three years after an attack of "erysipelas" of the forehead developed slowly-healing ulcers over the body and limbs. The ulcers appear to have been associated with a general bluish network, and to have arisen from the breaking down of nodules which appeared at the "knots" of the network. Father and mother were tuberculous.

Dr. Pringle, in 1902, showed at the Dermatological Society of London a case which he regarded as similar to Unna's case—Asphyxia reticularis multiplex.

(4) The next case of this sort was reported by Balzer and Griffon, in 1897, as "Inflammation avec pigmentation des réseaux superficiels du derme (Érythème pigmenté réticulaire)," with an additional note in 1898.

The patient was a man, aged 30 years, with a pigmentary mottling on the inner side of the thighs and knees and legs (which recalled that which is seen in persons who use a chaufferette), to which they gave the name "Érythème pigmenté réticulaire," and which they attributed to a rheumatic condition associated with varicosity of the veins. Lebelle afterwards discovered an hepatic cirrhosis in this patient, and Balzer and Griffon believed this to be a contributory cause of the skin condition.

(5) In 1907 Balzer and Merle recorded a second case in a man, aged 60 years, a diabetic, who had varicose œdema of the legs with eczema, and who presented a similar erythematous mottling to that of their earlier case. They concluded that it was an inflammatory affection which might be seen in individuals of defective nutrition, the subjects of functional troubles or of affections of the viscera, with marked embarrassment of the peripheral circulation.

(6) Bonnet, in 1908, exhibited the case of a man with intense generalised persistent violaceous marbling and who had mitral disease, and in 1909, in a review of the whole subject of Livedo annularis, he arrived at the conclusion that in certain individuals of defective nutrition, and especially among such as show a tendency to benign tuberculous lesions, there may be an exaggeration of the normal or physical Livedo annularis produced by cold in healthy subjects, and that the rare type described by Balzer is inflammatory, and may be associated with visceral disease or occur without evidence of such.

(7) Guillam and Troissier showed a case to the Société Médicale des Hôpitaux de Paris in 1909, in a man, aged 36 years, who had "Tabes fruste." Poncet and Queyrat regarded the condition as indicative of "lymphatic" or tuberculous tendency.

(8) Milian and Bouveyron also mentioned or showed cases to the same Society in 1909. Milian expressed the opinion that it was a tuberculous manifestation, and in Bouveyron's cases it was associated with hypothyroidea and a history of syphilis, an association which will be referred to immediately.

(c) *Livedo-like Eruptions Associated with Syphilis.*

(1) Wilson, in *Portraits of Skin Diseases,* Plate XXIV, described a case of livedo-like eruption in a syphilitic subject. The patient was a young married woman who had syphilitic condylomata four months after marriage, and a few months later red flat spots on the face, neck, back, arm, and three or four on the right leg. A month or so later she presented a peculiar mottling of the legs, which recalled to Wilson the "Ephelis ignealis" of French authors. The spots on the right leg seemed to be the starting point for the network at that part,

and Wilson regarded the affection as "Melanopathia syphilitica." Although Crocker states that Wilson erroneously attributed to syphilis a case of "Ephelis ab igne," it seems probable that Wilson was right, and that his case belonged to a class which has been since described by Ehrmann.

(2) Ehrmann, in 1907, in an article in the *Wiener medizinische Wochenschrift* ("Ein neues gefass Symptom bei Lues"), again in 1912, in the *Archives für Dermatologie* ("Weiter Mitteilungen über syphilitische Veränderungen der Hautgefässe und die damit zusammenhängenden Phänomene"), and again in his *Atlas der Hautkrankheiten und der Syphilide,* says that "Livedo annularis" or "Cutis marmorata" is often specially marked in drinkers who are exposed to cold and damp, and that if these persons contract syphilis there may develop from the second year onwards a syphilide, which he calls Livedo racemosa. He says also that the earlier large macular syphilide or recurrent annular macular syphilide is formed upon a basis of cutis marmorata, and that the brownish-red crescents and broken circles of this eruption correspond with the network of the cutis marmorata, from which they are distinguished by the fact that they fade less easily on pressure, and in that they tend to become more pronounced when the skin gets warm, whereas Livedo annularis disappears. When large macules are formed these are seen to correspond with the knots of the network.

This large macular syphilide is due, he says, to an endarteritis of the arterial plexus between the cutis and the sub-cutis, and that it may eventually lead, by escape of the spirochætes into the tissue around the vessels, to a later form of tubercular syphilide, which also takes the form of a broken network, and which he calls "Livedo racemosa." He gives drawings of both forms of reticular syphilide the "Roseola syphilitica recidivans annularis" (*Atlas,* Plate XLII, fig. 2) and "Livedo racemosa neben gruppierten tubercula syphilitica" (fig. 89).

Schmidt criticises Ehrmann's explanation of the pathology of this eruption, and says that the veins and not the arteries are affected.

Possibly we may put into this category of syphilitic livedo Wilson's case and Bouveyron's case, already mentioned, and a case recorded by Parkes Weber, as "chronic Reynaud's symptoms probably on a syphilitic basis, associated with Livedo reticulata."

(d) *Cases of Bazin's Disease presenting a livedo-like pattern.*

To this list of cases, which we may style "inflammatory Livedo annularis," I would propose to add a series which probably belong to the group of tuberculides of the type of Erythema induratum scrofulosorum or "Bazin's disease." I am not convinced that persistent and pronounced livedo indicates a special tendency to tuberculosis, but when tuberculides of the type of Bazin's disease occur in patients so affected the Erythema induratum occurs on or maps out the livedo network.

The cases to which I refer to occurred in girls of from 11 to 15 years of age, that is, at a younger age that the usual subjects of Bazin's disease. All had pronounced "chilblain circulation" and generalised Livedo annularis, and in some cases there was marked glandular enlargement or enlargement of the spleen. I believe these cases are merely examples of Bazin's disease in children who have marked livedo; but Dr. H. Morley Fletcher, who has observed several of them with me, is of opinion that the syndrome of symptoms, namely, Livedo annularis with a localised livedo-pattern inflammatory infiltration, the general glandular enlargement and the enlargement of the spleen, indicate a combined effect of congenital syphilis and of tuberculosis. In two cases a positive Wassermann reaction was obtained.

The following are brief notes of some of these cases:

(1) Mabel S—, aged 11 years, April, 1911. There is a general Livedo reticularis. The lower third of each leg below the knee is the seat of a circumscribed area of much more pronounced mottling in the form of an irregular network of bands of dusky red, which give a feeling of superficial infiltration to the touch (Fig. 3). In 1916, the girl now being aged 16 years, the general livedo is less, but the network-like "Bazin's disease" is rather more pronounced on the legs.

(2) Mary P—, school-girl, aged 13 years, March 13th, 1912. There is a general Livedo reticularis, with cold and blue extremities, and some pea-sized dusky-red nodules on the fingers, which suggest papulo-necrotic tuberculides (Acne scrofulosorum). On the legs, below the knees, there are areas of more pronounced dusky-red mottling, and on the feet some groups of pea-sized red-brown nodules on a dusky-red base. The glands on the left side of the neck are enlarged. *Diagnosis*: Livedo, Acne scrofulorosum, and livedo-like Bazin's disease on the legs. In 1916 I learn that the patient is in the Sea-bathing Infirmary at Margate for tuberculous glands in the neck.

(3) Maud H—, aged 11 years, December, 1912. There is a pronounced general

livedo. The glands in the neck are enlarged. On the forearms, thighs, and calves the livedo is still more pronounced. and forms here large areas of dusky-red mottling, with a slight feeling of induration (Fig. 4). On the forehead and cheeks there are dusky-red nodules in circinate groups.

In 1914 the patient was seen by Dr. Morley Fletcher. who reported that the Wassermann reaction was positive, and who suggested that the child had tuberculosis and congenital syphilis.

(4) Maud McC—. aged 12 years, March, 1912. The eruption appeared one year ago. together with pains in the joints and slight attacks of vomiting. She was admitted under Dr. Morley Fletcher. No visceral lesions were discovered. There was an evening rise of temperature (101° F. to 102° F.). which continued for about two weeks, and was accompanied by joint pains and a further eruption. The eruption consisted of irregular mottlings of a dusky-red colour upon the forearms, the inner sides of the knees, and the buttocks, with a dusky-red patch on the cheek. The mottling was in patches, and each patch had a broken network-like aspect. The network was slightly raised and slightly infiltrated, with here and there along the cords of the network red-brown pea-sized nodules. There were no enlarged glands. The patient was seen in June, 1916. The patches of dusky mottling was still present on the limbs, but the patch had disappeared from the cheek.

The case was exhibited at the Dermatological Society (*Brit. Journ. Derm.*, vol. xxiv, 1912, p. 324), with the diagnosis of "Bazin's disease."

(5) Lily G—. school-girl, aged 10 years, July, 1912. Eruption of two months' duration. On the outer side of the right arm and forearm. on left upper arm, on front of right knee, and on right calf there are areas of very deep purple mottling, the mottling being in the form of a network. There is also a general tendency to a less well-marked retiform mottling or livedo, and the network of the more decided patches corresponds with that of the livedo. In September, 1912, retiform patches appeared upon the thighs and buttocks. The patches on the arms and legs now form dusky-red areas, with a darker retiform mottling, and with several pea-sized red-brown nodules situated deeply in the skin along the bands of network. There are no enlarged glands. Von Pirquet reaction, positive. Microscopical examination of a section of an excised nodule showed round-cell and epithelioid-cell infiltration round the blood-vessels of the derma. This case was shown at a meeting of the Dermatological Section on October 17th, 1912 (*Brit. Journ. Derm.*, vol. xxiv, 1912, p. 394), as an example of "Sarcoid of Darier." In June, 1912, there was no change.

(6) Louisa K—, aged 12 years, October, 1915. There are very numerous and much enlarged glands on both sides of the neck. and incision scars where some glands were removed two years ago. The hands and feet are dusky and cold, and there is a pronounced general Livedo reticularis. On the calves and sides of the legs there are large areas where the livedo is much more pronounced, and forms a dusky-red network, which gives a feeling of infiltration, while here and there in the network there are obvious nodules, some of which have broken down into punched-out ulcers (Fig. 5). The spleen is distinctly enlarged. *Diagnosis*: "Bazin's disease," with livedo-like distribution.

On June 14th, 1916, there was no change, except that there were no actual ulcerations.

IV. Livedo annularis as Suggesting an Explanation of the Patterning of Certain Common Eruptions.

Finally, I wish to refer to the manner in which the circulatory system of the skin, as we see it mapped out by Livedo annularis, serves to explain the distribution of certain common eruptions apart from the more frankly reticulated eruptions already mentioned.

It has been suggested by Bonnet that the macule of syphilitic roseola corresponds to the "area of maximum circulation" or to the mesh of the network; but from my own observation I am inclined to the view that both macules and papules of secondary syphilitic eruptions in persons with livedo correspond to the knots of the network as shown in the diagram (Fig. 6), and I am convinced that this is so, at any rate for the papules. An explanation of this circumstance would be that the spirochætes get "hung up" just at the points where the circulation is most feeble, and there give rise to a reaction.

In a similar manner one sees in a case of Bazin's disease that the nodules always occur at the knots of the network of livedo, and, as in the cases I have described above, they may often extend along the rest of the network to form a reticulated pattern.

The Livedo racemosa of syphilis of Ehrmann is probably due to a similar extension of the syphilitic infiltration along the livedo network.

It seems very likely, too, that the spaced arrangement of other eruptions may be explained in just the same manner: that of morbilli, for example, as is suggested by the illustration in the *Jacobi-Pringle Atlas* (Plate LVI). And Fox and Macleod have noted how the eruption of Parakeratosis variegata and of Lichen planus sometimes takes the form of the livedo network.

Conclusions.

To sum up our knowledge of Livedo annularis:

(1) The dusky marbling or network known as Livedo annularis is a result of the tuft-like arrangement of the blood-vessels of the skin as demonstrated by Renaut. The network corresponds to the regions of "reduced circulation" between the tufts.

(2) It occurs as a normal condition in many children and young adults, and is exaggerated as a result of exposure to cold.

(3) In departure from health due to tubercle, syphilis, rheumatism, alcoholism, hypothyroidism, etc., the normal Livedo annularis may become exaggerated and persistent, possibly, as has been suggested, from a toxic action upon the splanchnic plexus.

(4) In such persons with persistent and exaggerated livedo the position and pattern of eruptions due to syphilis or tubercle may be determined by the livedo, so that the eruption takes a network aspect and may be called "inflammatory livedo."

(5) A similar inflammatory livedo, with subsequent pigmentation, may be produced by prolonged exposure of the skin to heat—"Livedo a calore."

(6) The distribution and arrangement of certain eruptions, such as those of secondary syphilis, of measles, of Parakeratosis variegata, and perhaps of others, is explained by the anatomical arrangement of the blood-vessels of the skin which gives rise to Livedo annularis.

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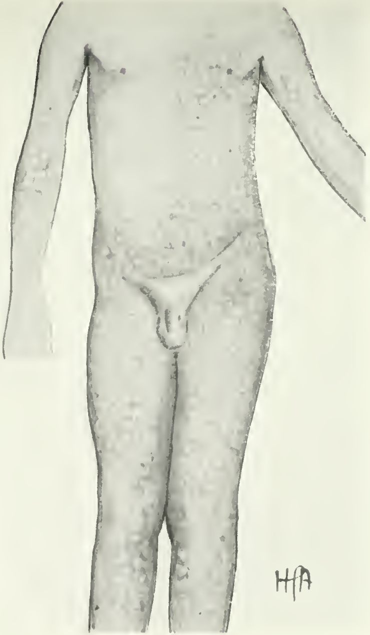

FIG. 1.

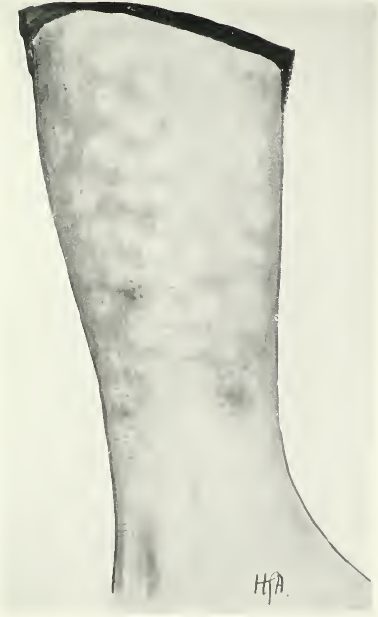

FIG. 3.

TO ILLUSTRATE DR. H. G. ADAMSON'S ARTICLE ON LIVEDO RETICULARIS.

[*To face p.* 294.

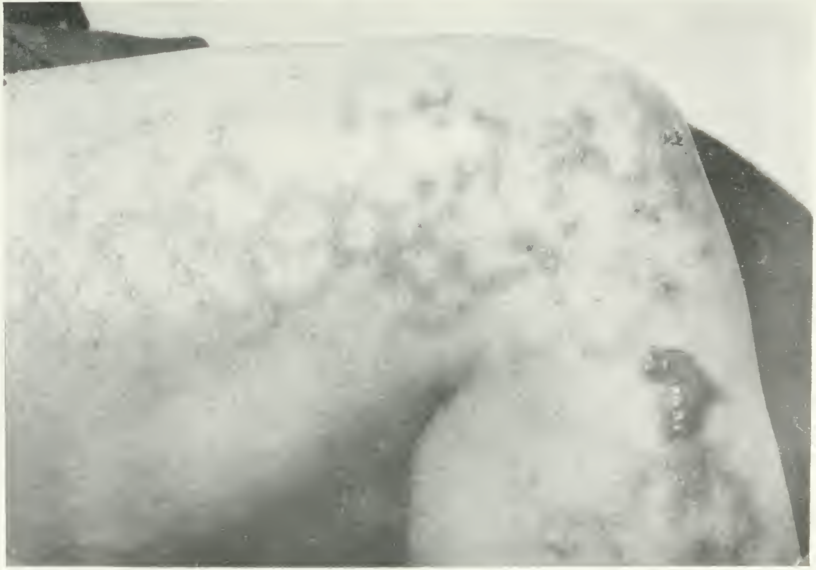

FIG. 2.

TO ILLUSTRATE DR. H. G. ADAMSON'S ARTICLE ON LIVEDO RETICULARIS.

[*To face p.* 292.

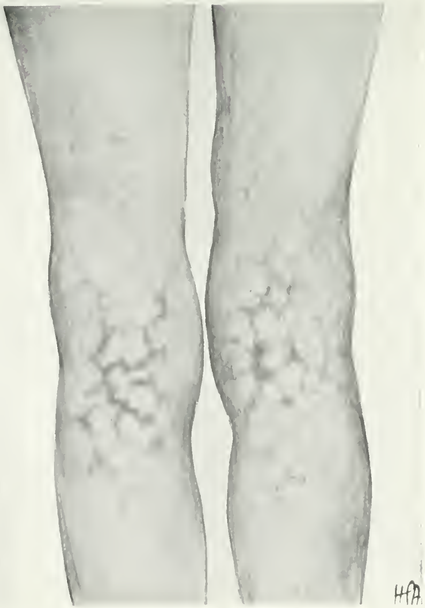

FIG. 4.

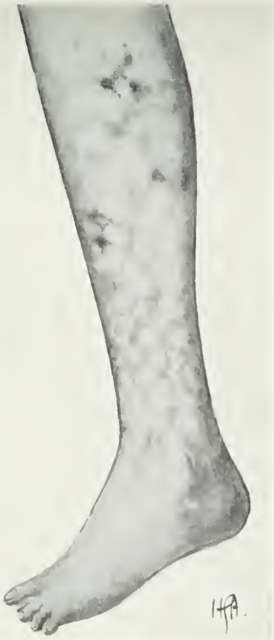

FIG. 5.

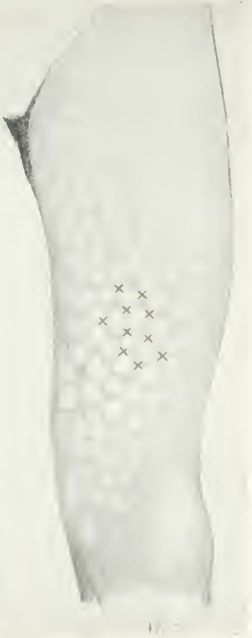

FIG. 6.

TO ILLUSTRATE DR H. G. ADAMSON'S ARTICLE ON LIVEDO RETICULARIS.

[To face p. 292.

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Explanation of Plates.

Fig. 1.—Livedo annularis, generalised, except that the upper half of the trunk on the right side was normal in appearance and showed no trace of Livedo annularis, which was elsewhere pronounced. The boy had hemi-hypertrophy of the face; the left ear and adjacent parts were considerably larger than on the

right side. This case seems to point to Livedo annularis as being a congenital anatomical departure from the normal rather than an acquired condition, the result of disturbance of the vaso-motor centres. If the latter were the case it is difficult to see why a large segmental area should be uninvolved.

Fig. 2.—Erythema ab igne.

Fig. 3.—Bazin's disease with Livedo annularis, showing how the nodules arise at the knots of the network (Case 1).

Fig. 4.—Inflammatory Livedo annularis with nodular infiltration at the knots of the network (Case 3).

Fig. 5.—Bazin's disease with Livedo annularis, showing how the nodules arise at the knots of the network (Case 6).

Fig. 6.—Diagram showing how the papules of a secondary syphilide correspond with the knots of the livid network. The x's are placed at the site of papules.

RADIUM TREATMENT OF LUPUS VULGARIS.*

(*From Finsen's Light Institute, Copenhagen* (*Director: Dr. Axel Reyn*).

By PAUL HASLUND,
First Assistant in the Institute.

Gentlemen,—No doubt you remember the increasing wave of enthusiasm for radium as a means of curing disease which about four year ago passed over great parts of Europe, and even with us in Denmark nearly carried away common sense and our naturally rather well-developed scepticism, until it met with a wall of criticism founded on quickly-acquired experiences of our own. For some time this swell was rather high, but latterly a dead calm has prevailed, during which it is to be hoped that a more sober view of what this marvellous substance is able to do may be settled. It was remarkably late that this transport of enthusiasm appeared to be unfounded, more than ten years after the introduction of radio-active bodies into the service of therapeutics. It brought, however, to the Finsen Institute the invaluable advantage that we, through the generosity of Mr. Jorgensen, obtained possession of a quantity of radium sufficient to enable us to make independent therapeutic observations instead of having to be content with the *rôle* of passive spectators, who without criticism had to accept what more or less enthusiastic and more fortunate practitioners of this expensive therapy chose to indoctrinate the world with.

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* This lecture was to have been delivered at the third meeting of the Scandinavian Dermatological Society, Christiania, June, 1916; but it was never given owing to the author's death directly before the meeting.

Since January, 1913, the Light Institute has possessed 2½ ctgr. of radium, distributed between three plate-apparatus and a tube. This quantity is, indeed, not overwhelming, and its smallness has, of course, influenced the extent we have been able to give our experiments. It was, of course, before all our duty to apply the new means to Lupus vulgaris, and try to make out whether it was able to compete with, or perhaps even to outdo, the weapons used till then in the fight against this disease, so telling on society and the individual. But, besides this, other tasks were quickly put to radium therapeutics also by our *clientèle,* so that, as a matter of fact, in the fully 260 patients treated with radium at the Institute there were only a relatively small number with Lupus. The results obtained with these, of which I am going to give an account, fully justify, however, my opinion that the *sphere of radium therapeutics with us has been quite different from what was anticipated at the outset.*

The enthusiasm for radium as a means of curing disease has in Lupus vulgaris, no doubt, never reached such a pitch as when it was the question of treating malignant tumours. But in this domain also an enthusiastic view has not been wanting in certain quarters. However, at the time when we were going to begin our experiments, the opinions existing about the action of the Becquerel rays on this disease were greatly at variance with one another. Owing to this fact, together with what we had had the opportunity of seeing elsewhere of the results of the treatment, we did not start with too great expectations. Consequently we have not been exposed to great disappointments; but, on the other hand, it may have contributed to a greater reserve in the selection of cases and to a limitation of the experiments as little by little it appeared that our new experience did not in any great degree encourage us to change our view.

Danlos seems to have been the first who, as early as 1900 and the following years (*Annales de Derm. et de Syph.*, 1902, pp. 493 and 723), recommended the use of radium in Lupus vulgaris. He was quickly followed by Hallopeau and Gadaud (*Annales de Derm. et de Syph.*, 1902, p. 720). Although the literature about radium published since then which deals with the question of lupus treatment is anything but overwhelming, I shall here only mention some few works in order to illustrate the constantly varying opinions. From the very outset two authors are apparently in absolute conflict with one another. Halkin (*Archiv f. Derm. u. Syph.*, Bd. 65, 1903, p. 201) states, as the result of his experiments, that the necrotisation of the surface and the deep action in radium treatment are not in such a relation to one another that it seems worth while to introduce the therapy in the case of Lupus vulgaris. By microscopic investigations he was also unable to find any action on the deep Lupus foci. Shortly after, Strassmann (*Arch. f. Derm. u. Syph.*, Bd. 71, 1904, p. 419), on the contrary, stated that by means of a treatment that was much less destructive to the tissues he was able to obtain the same results, *i.e.* actual healing of the lupus process which others had seen only after destructive doses. He consequently concluded that a simple reactive inflammation is sufficient to bring about the cure, and that lengthy exposures are not suitable to the treatment of Lupus vulgaris. Microscopically nothing was demonstrable that could be said to suggest a specific action on the lupus nodules.

Wichmann (*Monatsheft f. prakt. Derm.*, Bd. 43, 1906, p. 687) finds an explanation of these two incompatible opinions of the value of the new treatment in the faulty technique used by Halkin, whereas Strassmann, no doubt unwittingly, had worked with filtrated rays, which, according to Wichmann, can alone be taken into account. He quotes 15 cases of Lupus vulgaris treated with good results in support of filtration. With regard to the introduction of this method into the technique in 1905, Wichmann tries in the face of Wickham, Degrais, and Dominici, who especially have worked it out, to maintain a claim of priority. For the rest, he is consistently one of the most enthusiastic advocates of the radium treatment of lupus. As late as 1911 (*Radium in der Heilkunde*, Hamburg-Leipzig, 1911) Wichmann is obliged to admit that till now no extensive statistics exist on which to establish a well-founded judgment, but that publications that report unsuccessful results are not wanting. Wichmann himself reported at that time 30 cases, observed during a rather extensive period, that had been treated with radium, either exclusively or combined with another treatment. Of these a very large proportion had been cured without relapses during four years. However, in his opinion, the treatment can only be taken into consideration in cases of rather small lupus foci. Later Wichmann communicated 112 cases of Lupus vulgaris with 44 cures, observed from one to fifteen months after mesothorium treatment, partly, however, in conjunction with some other treatment (*Strahlentherapie*, Bd. 1, 1912, p. 483).

Kuznitzky (*Arch. f. Derm. u. Syph.*, Bd. 116, 1913, p. 423) does not share Wichmann's favourable view of radium therapeutics in the case of lupus. His own results with mesothorium were anything but encouraging. Personally I have no experience with this substance, but both the authors named consider its action as at least equal to that of radium.

Wickham and Degrais, who during six years have treated about 200 patients suffering from tuberculosis, of whom a great many must be supposed to have had lupus, are among those who have the greatest experience in this domain (*Radiumthérapie*, Paris, 1912). They are very reserved in their conclusions. To begin with they obtained good results; but in the course of time the occurrence of numerous relapses have taught them to draw more prudent conclusions. Lupus vulgaris is not liable to any selective action, and the nodules in the ulcerated tissue are especially resistent. They must be treated to a certain extent by destruction with radiation through lead filters of the thickness of $\frac{1}{10}$ mm. to $\frac{3}{10}$ mm. For the deeper infiltrated layers a medium filtration is suitable and lupus ulcerations had better have inflammatory doses. Wickham also made a careful study of the histological alterations caused by the treatment (with Bellot, *Strahlentherapie*, Bd. 3, 1913, p. 64).

We meet with a more favourable view from Barcat (*Précis de Radiumthérapie*, Paris, 1912; *Strahlentherapie*, Bd. 4, 1914, p. 322). He states expressly that no cure was obtained by ultrapenetrant radiation after the manner of Dominici. On the contrary, working with $\frac{1}{10}$ mm. lead and 2 mm. cellulose filter in sittings of up to forty-eight hours he obtained very noteworthy results after three to four series. The cure, however, does not always last. A cosmetically fine cicatrisation is said to be obtained, but Barcat has a clear understanding of the fact that telangiectases occurring later have to be reckoned with. According to his statements in another place the dosage used must also have caused an erythematous-ulcerous reaction of three to four months' duration.

Riehl and Schramek (*Wien. klin. Wochenschr.*, 1913, No. 37) work in accordance with Pfannenstiel's principle by combining radium treatment with the intensive use of iodide of potassium, and, without speaking of lasting cures, they consider this method superior to light-treatment as far as certainty and quickness are concerned. I confess that I do not understand their way of reasoning. Indeed, a quite simple experiment will quickly show that radium is altogether unable to split iodide of potassium. And if it were thinkable that the splendid action was due to this substance only, one cannot help doubting the correctness of their diagnoses.

Lautsch (*Sitzung des Lupus-Ausschusses des deutschen Zentralkomitees zur Bekämpfung der Tuberkulose,* Berlin, 27 Oktb., 1913, *Ref. Derm. Wochenschr.* 1913, Bd. 57, p. 1411) has got very good results by using medium filtration; but according to his experience lesions of the mucous membranes give the most important indication for the treatment. Without expressing any general judgment of the value of the treatment, Jungmann contents himself with calling radium a radical means of curing disease, especially suitable to lupus of the mucous membranes and the colliquative forms on the skin, but which can by no means replace the Finsen treatment (*Strahlentherapie,* Bd. 4, 1914, p. 221). This latter point is also strongly emphasised in the report of the London Radium Institute of 1913 (*The Lancet,* 1914; *Strahlentherapie,* Bd. 5, 1914, p. 12). Hayward Pinch here states as the result of his experiments that the Finsen treatment is preferable to radium, which he applied without filtration with exposures of one to two hours to bring about the destructive reaction he considers necessary.

As you will see from these examples, there is not overmuch harmony of opinion either with regard to the value of radium therapeutics in cases of Lupus vulgaris or on the purely technical question of the most efficient way of administering Becquerel rays in this disease. In spite of the many years that have elapsed since Danlos initiated the new treatment, we have practically not as yet got beyond the experimental stage, and shall hardly do so till further biochemical experiments on the action of radium are at our disposal, which will most likely lead to an expedient alteration of the technique as used till now as provisionally the only practicable one. This technique, the rational application of which is anything but easy, and which may change from case to case even in the same disease, is founded on the unequal absorbability of the different qualities of rays in connection with a selective action on pathologically altered tissue, having regard to the destructive processes which all qualities of rays are able to bring about when acting during a suitable time in proportion to their quantity. Our knowledge of these and other data important to the therapy is, however, still deficient. Thus while Wickham, as already stated, got no impression of selective action on lupus tissue, Wichmann states that the latter absorbs more than twice as much of the rays as the bordering healthy skin. Further, Wichmann considers absorption still possible to the depth of 2 cm., which is of importance in the case of an infiltrative disease like Lupus vulgaris, whereas Kutmann and Meyer more precisely state that the rays, at the utmost, penetrate to the depth of 7 mm. or 8 mm., whereas the rays are absorbed by all layers of tissue losing about 10 per cent. per centimeter they pass through (*Strahlentherapie*, Bd. 3, 1913, p. 744).

Remembering, finally, what Barcat indicates as applicable to any kind of radium treatment, viz. (1) that each apparatus has its peculiarities; (2) that the power of resistance of the patients varies greatly; (3) that as a rule pathological tissues can stand much higher doses than healthy ones; (4) that it is of the greatest importance whether full doses are given or the treatment is fractional; and (5) that the dose, after all, is dependent on the radiation surface of the apparatus, in other words weakens in proportion as this surface diminishes, we are hardly going too far in stating that *the whole therapy is, and provisionally must be, a purely empirical one.* This does not exclude the fact that in some few diseases a certain technique has already been fixed as the most suitable one. But, as far as Lupus vulgaris is concerned, this is, as we have seen already, not the case.

In all we have tried radium treatment in 31 cases of Lupus vulgaris of the face, besides some with lupus of the mucous membranes, treated by Dr. Ove Strandberg, and which I shall here leave out of consideration. With a few, however, of these patients the treatment was not carried through with sufficient persistence, partly because their cases apparently at once got worse, although scarcely ever owing to radium; partly from quite external reasons, it being difficult to make the patients turn up regularly, or according to their own wishes, which we, from our view of the therapy as stated above did not think there was any reason to set our face against. The material, however, was sufficient to allow us to form a well-founded opinion of the action of radium on Lupus vulgaris. I am now going, quite briefly, to report to you a number of our cases in order to show the result at which we have arrived.

(1) In a single case, a boy aged 9 years, the radium treatment has been applied by itself. He had on his left cheek a scar of 2½ × 1½ cm., of which a portion, the size of a pea, showed typical lupus spots. He was never treated by light. After two and a half months only traces of the nodules, as a quite slight pigmentation, were visible, and the radium treatment was stopped after six series at intervals of from eight to fourteen days up to one month. Three months later the scar was smooth and soft without signs of disease, the lower part, however, slightly pigmented and desquamating. After repeated observations till January 20th, 1914, thus two and a half years after the cessation of the treatment, no nodules were visible, the scar being somewhat atrophied with fine telangiectases. Several times some reaction had occurred, with redness and superficial excoriation after treatment.

With all the other patients light treatment was applied, with some of them also X-rays, and with a few electrolysis treatment after the manner of Reyn, the radium treatment having either replaced the previous treatment entirely or in some areas, or been tried simultaneously with the latter from the very beginning in different places. In this way we expected to get the surest impression of which treatment, in a given case, was able to yield most, radium not having been reserved alone for patients in whom the therapeutics had not previously produced the desired progress.

(2) Lupus vulgaris treated with light from 1910 and greatly improved. A new nodule in a scar on the neck was treated with radium from April 23rd, 1913, the light treatment being otherwise continued. After but three series, at intervals of four and three months, the nodule seemed to have disappeared (June 9th, 1914), it being possible only to show some desquamation in the scar. About seventeen months later still no signs of disease. A distinct light reaction, such as increased redness, had appeared after the treatment.

(3) Lupus vulgaris on the nose and below the chin in a scar after glandular suppuration. Light and radium treatments began nearly simultaneously, the latter on April 23rd, 1913, on the spot below the chin, where also numerous little nodules were to be found. Seven months later (November 21st, 1913) there were still a certain number of nodules, whereas the scar after light treatment on the nose, was free. Still two years later, after another six series at intervals of two, five, and twelve months, there were, on November 10th, 1915, traces of nodules on the part treated with radium, whereas on the nose there were still no signs of disease. After radium a very vigorous and persistent reaction occurred, with superficial ulceration, the scar afterwards appearing somewhat atrophic.

(4) Lupus vulgaris spread on left cheek below the ear and on the neck, partly ulcerated. Light (later also X-rays) and radium treatments started simultaneously, the latter on February 4th, 1913, on a spot below the chin, with

hypertrophic nodules, of which some ulcerated. In the course of nine months five series, at intervals of three weeks—two to three months, were applied, and fully one year after the beginning of the treatment there were hardly any symptoms of disease on the spot, whereas nodules were still to be found on the parts treated with light and X-rays. After another year no relapse on the spot treated with radium, but otherwise still lupus areas to which then also radium was applied. Six and a half months later, after three series at two to three months' intervals, there were still nodules here. The reaction after the treatment was generally vigorous and persistent with ulcerations.

(5) Lupus vulgaris on nose, left cheek, and neck. Radium treatment started on February 7th, 1913, about simultaneously with light treatment on a spot reaching from the maxillary angle down on the neck to the extent of 6 × 2 cm. The middle part was scarred, but at both ends confluent infiltrations and nodules were found. These areas measured $2\frac{1}{2} \times 2$ and $1\frac{1}{2} \times 1$ cm. respectively. Apparently the affection improved remarkably quickly both on the spots treated by light and on those treated by radium, and for a time it seemed healed. But partly ulcerated nodules reappeared in the scars. After twenty months there were no distinct nodules on the nose nor on the spot to which radium was applied, only a little desquamation in its foremost part. Four months later another ulcerated nodule of a size of a lentil on the nose; on the neck no nodules, but an ulceration after the last radium treatment, and here the existence of a nodule was ascertained fully three months after. Four and eight months later, thus after nearly three years' treatment, cure seemed obtained after in all nine series at intervals of three weeks, two, three, and six months, accompanied in parts by a vigorous and persistent reaction, on a few occasions by an ulceration necessitating light treatment to produce healing, and pronounced atrophic cicatrisation.

(6) Lupus vulgaris, light treated from 1898; later electrolysis and X-rays have been tried. The affection progressive if anything, partly ulcerated. On March 24th, 1914, two new nodules on the neck were noticed, one of which was ulcerated; from March 31st, 1914, radium was applied to them. One year after numerous nodules had appeared on one of the spots treated with radium, on the other a single nodule remained. About six months later things were practically unaltered after in all four series at intervals of six to seven months. A very considerable reaction had occurred after radium, lasting about two and a half months.

In these six patients radium was thus applied to rather early and limited lesions, which had not been otherwise treated before. The other cases I am going to report here had, on the contrary, all of them an old and widely-spread lupus, on which the light treatment either acted very slowly or without any satisfactory effect, or in which a cosmetically good result had been obtained by the latter treatment apart from a few resistent areas. With those it seemed worth trying whether radium would be able to accelerate cure and, as it were, carry us beyond the dead-centre.

(7) Widely spread ulcerative Lupus vulgaris, light treatment applied from 1898; the remaining ulcerations treated of late with Reyn's electrolysis. On March 27th, 1913, there still remained four ulcerations of ½ to 1 cm., somewhat flattened after the treatment. Radium applied.

The case to begin with improved rather well, so that seven months later there was no more ulceration, but still infiltration and nodules in the scars. New nodules and a single new ulceration also improved. At a given time, about eleven months later, there were altogether no definite symptoms of disease: the scars smooth, soft, slightly depressed. However, new nodules and ulceration reappeared, but after another nearly fifteen months' treatment everything was again, for a while, apparently healed. Three years after the beginning of the treatment the state was not yet good, nodules and an ulcer the size of a pea having reappeared on the nose, while some of the treated parts remained healed. The patient had had in all ten series at intervals of one, two, three, four, seven, and nine months. There was always a vigorous and persistent reaction, leading to the formation of somewhat depressed scars with some telangiectases.

(8) Lupus vulgaris, widely spread, light applied from 1902, and considerably improved. A few resistent spots, which later had also been electrolysed. From September 24th, 1913, radium was applied to a few spots on the nose and right cheek. To another in the same place and one on the temple light was applied. The spots treated with radium seemed to take a long time to become those least affected. Anyhow, after nine months, one of the spots to which light had been applied had healed. Fully seven months later there were still nodules to be found in the spots treated with radium and in one of those to which light had been applied. After another three months' treatment no more radium was applied, but light only on all the remaining spots. After this nodules were still to be seen eight months later. After the radium treatment, in all ten series, at intervals of one to three months, vigorous reaction occurred, several times with superficial persistent ulceration accompanied by pain and soreness, and the scars were atrophic with telangiectases.

(9) Lupus vulgaris, light treated from 1900, and almost healed except a very resistent spot at the lobe of the attachment of the right ear. This spot was treated both with light and X-rays till, on August 24th, 1914, radium was applied as nodules constantly remained. After six series, at intervals of two, three, and five months, lasting in all thirteen months, there was an unquestionable improvement; but when the patient returned fully four and a half months later there was still indubitable lupus infiltration, which was again treated with light. Reaction has been powerful, with a superficial necrosis and severe pain after radium treatment, and the scar was markedly atrophic with telangiectases.

(10) Lupus vulgaris, greatly improved by light treatment from 1904. However two resistent nodules remained in the scar, one which was continually treated with light, whereas radium was applied to the other from January 29th, 1914. Six months later the nodules still existed after four radium treatments at intervals of one to three months. Each time there was reaction, with superficial excoriation and soreness.

(11) Widely scattered Lupus vulgaris, greatly improved by light treatment from 1897, but still presenting resistent parts, to which electrolysis had also been applied. On February 3rd, 1914, radium treatment was started on a scaling lupus spot, the size of a hempseed, in a patch on the right cheek. One year later

there still remained a small desquamating nodule, and after another eight months the nodule had not quite disappeared after seven series, at intervals of two, three, and five months, followed by a rather strong reaction.

(12) Widely scattered destructive Lupus vulgaris. Light applied from 1902. On April 22nd, 1913, radium was applied to the upper lip on a partly ulcerated, partly lupous area of 1½ cm. For the rest, the light treatment was continued, later combined with X-rays. After but two series, at the interval of a little more than a year, the ulceration had healed, and the state was, on the whole, good ; however, a few nodules still remained.

(13) Lupus vulgaris, light treated from 1899, and on the whole improved, but numerous nodules still remained in the scars, and in certain places the lesion had spread. From February 6th, 1913, radium was applied to a spot above the left eyebrow, the light treatment being continued elsewhere. To begin with, apparent improvement. Later on an ulceration formed superficially on the spot, which still remained about six and a half months later, while deep-seated nodules continually persisted. After in all five treatments, at two to two and a half months' interval, which had been followed by strong reaction, with superficial ulceration of rather long duration, the part was treated with light. Later the patient also got light baths, but after two years and three months there were still a few nodules upon the left eyebrow.

(14) Lupus vulgaris on the nose, having improved by application of light from 1903 ; but an ulcer remained, to which also electrolysis, after the manner of Reyn, had been applied. On May 21st, 1913, the ulcer on the left ala nasi measured 1 × 1 cm. It was rather deep, with swollen edges. So a radium treatment was tried. A couple of months later the ulcer had enlarged, but was more superficial, and after another four months it was still larger. After in all five series, at intervals of one to two months, the state was, on the whole, on January 8th, 1914, bad, there being two wounds of 1½ × 2½ and 1½ × 1 cm. respectively. After this light treatment only was re-applied, and ten months later no lesions could be ascertained on the nose. We were unable to observe the reaction of the radium, the patient each time going home.

(15) Widely scattered Lupus vulgaris, improved partly by light treatment from 1910 and partly by X-ray treatment. There were, however, still some refractory parts. From May 13th, 1913, radium was applied to an ulcerated nodule of the size of a lentil on the left cheek. Fully three months afterwards there were no more distinct nodules to be seen on that part after only three series, at intervals of one month ; and more than fifteen months later there was still no disease in the place. In the spots treated with light a single ulcerated nodule was visible, otherwise these two had apparently healed. After another similar space of time there were, however, on February 22nd, 1916, relapses everywhere ; simultaneously the patient's general state was becoming worse, and, in the course of a short time, death occurred, owing to a pulmonary tuberculosis. The radium treatment had caused a strong reaction, with redness, ulceration, and a membranous surface, and the scars afterwards were slightly atrophic.

(16) Lupus vulgaris, widely spread, and constantly relapsing, with ulcerations. Light treatment applied from 1898. On May 18th, 1913, radium treatment was started on a few closely aggregated nodules on the cheek above the border of the left jaw. Fully seven months later nodules still remained, both on the parts treated with light and on the spot treated by radium, and more than a year

later the state was, on the whole, unaltered, new nodules and ulceration reappearing everywhere. In all the patient had received six series, at one to three months intervals. A very strong and persistent reaction, with ulcerations, œdema of the surroundings, and pain followed.

The last two patients I am going to speak about had both a widely scattered lupus which, in spite of many years' treatment with local or temporary improvement, went on spreading and constantly relapsing by the formation of new nodules and ulcerations on apparently healed parts. In both cases the disease presented quite flat but evidently deep lesions, and although on the face of it they did not seem suitable for radium treatment, we yielded to the wishes of the patients to try this treatment, the results obtained by the Finsen treatment being, as already stated, most unsatisfactory.

(17) From 1898 light treatment had been applied to the patient's Lupus vulgaris, but, owing to the small progress, she had for some time given up all treatment. From January 18th, 1913, radium was applied to her, first to a limited part, afterwards all over the lesion, which was almost coherent, and reached across the greater part of the left half of the face, left ear, and down on the neck. An indubitable improvement occurred, with flattening and increasing cicatrisation of the parts treated with radium, but it was evidently only temporary, new nodules constantly reappearing, and the lesion spreading to parts of the skin that, as yet, had not been affected. After fully a year, the light treatment was taken up again, together with radium, and, after repeated series, at intervals of two to six months, all this was at last given up, having been tried in all for more than fifteen months. Later on, by continuous light treatment, combined with universal arc-light baths, a very considerable improvement has been obtained in the course of a year. There are, however, constantly fresh outbreaks here and there. After radium there was, as a rule, a distinct or strong reaction with superficial necrosis, local soreness, and spontaneous pains in parts.

(18) Coherent Lupus vulgaris on the nose, the whole of the face down on the neck, with considerable hard fibrous cicatrisation in places after light treatment from 1897. There were, however, constantly numerous large and small nodules and infiltrations spread over the parts affected, but only here and there quite superficial ulceration. This patient, too, had renounced light treatment. from which she did not expect further improvement, but she now carried through the radium treatment, which began on January 17th, 1913, with a touching energy. After the course of about one year there was still no manifest improvement, but later on gradual healing was actually obtained, so that after numerous series, at intervals of one, two, and three months, nearly uninterrupted for more than three years, there are now only distinct lupus nodules or small infiltrations with firm desquamation in some few scars. As a rule there was a strong reaction, with marked redness, dry desquamation, or superficial necrosis, persistent, and often appearing rather late. The cicatrisation is markedly atrophic, with many telangiectases and tension of the tissues, so that the cosmetic result cannot be called satisfactory.

These examples will suffice to illustrate the action of the treatment. As to the technique, it may be said generally that, especially in the beginning, it was somewhat variable, not only in different cases, but also with the same patient from one application to another. Considering the great variations of the statements of dosage from an application *à nu* (the English Radium Institute) to the use of medium or still greater filtration (Barcat), there was nothing to do but to proceed by way of experiment to the greatest extent possible. We have, however, only a few times tried a treatment without filter (*i. e.* with only a couple of layers of india-rubber over the preparation) in sittings of twenty minutes with a single patient who complained strongly of painful reactions. Otherwise we used partly a weak filtration consisting of two layers of india-rubber and three to five layers of paper or india-rubber and $\frac{1}{20}$ mm. to $\frac{3}{20}$ mm. of lead-foil and rather short sittings; partly and more frequently a medium filtration with india-rubber and $\frac{1}{4}$ mm. or more rarely $\frac{1}{2}$ mm. of aluminium or lead, in some cases with addition of cellulose (five layers of paper) and wadding-filters ($\frac{1}{2}$ cm.) to keep out secondary rays, for a somewhat varying period. From practical reasons we have always given the treatments in fractional doses at intervals of one or two days, and as a rule, in cases of superficial nodules or infiltrations, combined with weaker or stronger filtration, or else first tried one form of treatment and afterwards gone on with the other. The duration of the whole treatment then varied between two and a half, three, four, six, seven, and nine hours distributed through two or three sittings. In a few cases we tried a filtration with two layers of india-rubber, $\frac{1}{2}$ mm. of aluminium, five layers of paper, and $\frac{1}{2}$ cm. of wadding for twelve hours distributed through two days.

It is difficult to decide with which combination of rays greatest results were obtained. Thus for the little boy I mentioned to you (Case 1), and whose lupus seems to have healed after six treatments, a combination of weak and medium filtration was used, while a similar dosage in other cases proved ineffectual or nearly so, and the reactions after these doses varied in intensity, though as a rule they were strongly pronounced. On the other hand, we have obtained unquestionable improvement both by exclusive radiation with weakly filtrated rays (*e. g.* Case 12) and by constantly using medium filtration (*e. g.* Cases 9 and 11) without obtaining healing; but not less frequently the results of both treatments were highly unsatisfactory. It seems as if ulcerative forms may sometimes easily be healed by relatively weakly filtered rays. At the same time one should not forget that the more penetrating rays also act, and now and then evidently sufficiently. But to act on persistent deep infiltrations the rather long application of the latter will as a rule be required, a thing that can only be done by interposing thicker filters. That is why it seems to me rational to use, as we often did, the above-mentioned treatment with unequal combination of rays, giving first, for instance, a mixture of softer and harder rays, to continue exclusively with harder ones in the same sitting, only applying, if wanted, the more penetrating qualities at the later series of treatments. I take for granted that the latter yield most in the case of quite close and deep lupus nodules. But beyond this I think we cannot go, on the basis of our experience, in the question of the most efficient form of applying radium rays in the treatment of Lupus vulgaris, among others for the reason that our results were on the whole not especially encouraging. Each case gives in many ways occasion for a constant variation of the finer details of technique.

As will be noticed from the cases reported, the treatment has always given rise to a distinct reaction, in this way, however, that it did not necessarily reach the same intensity after each series. It, of course, depended to a certain degree on the dosage chosen for each sitting—that is, on the combination of rays and the time during which it acted. But my experience will not allow me to think that there is any prospect of being able to make valid calculations of the degree of reaction that could be expected in each particular case, when these factors are duly taken into account. Circumstances out of one's reckoning, such as the quantity of pathological tissue and the different susceptibility of the patients, and perhaps of the local areas, all circumstances which, moreover, are subject to changes in the course of the treatment, may possibly here be of consequence. Sometimes we have observed a weak "ante-reaction" such as a weak evanescent redness immediately after the treatment and quickly passing. The typical radium reaction was always rather long in appearing, and in a few cases it did not appear till very late indeed. Sometimes it only manifested itself by a limited marked redness with a more or less pronounced dry desquamation; but most frequently it caused at the same time a superficial necrosis, with grey-yellowish surface or excoriation and flat ulceration. Only on a few occasions was a deeper wound formed, healing by light treatment. Otherwise the reaction in many cases lasted very long, up to several months before quite disappearing, and, what is worth noticing, in not a few cases it was, besides by local soreness, accompanied by spontaneous pains that were most troublsome, exactly as in the case of an X-ray ulcer. Such pains may occur, even if no ulcerations are formed, a fact we have also noticed in the treatment of other diseases than Lupus vulgaris. On the other hand, the pigmentation which generally so easily follows radium treatment has seldom appeared, and then only of very slight intensity.

These reactions with superficial necrosis and ulceration, which do not always of necessity annoy the patients themselves, contribute, of course, to delay the treatment much more than the reaction which follows on light treatment. The only way of avoiding them is either by using a still stronger filtration, when, according to Barcat's investigations, the effect is lost, or by shortening each sitting rather considerably; but then it is a question whether the same result is obtained by numerous and frequently repeated applications. According to Strassman's researches, that are already somewhat old, this should seem possible; but to judge from the defective information which we generally get on this point, later radium therapeutists find it on the whole more advantageous to use a technique that cannot but give rise to such reactions as those we have seen. The question can hardly be solved by theoretical considerations only. It is certainly only very rarely that cures are obtained by a direct destruction and expulsion of the lupus foci, and of course only when these are quite superficial. Much greater influence is attributable to the deep reactive inflammation of which the necrosis of the upper layers of the skin is the visible outcome. It is rather doubtful whether this deep action, which is scarcely due to the qualities of rays penetrating into the tissue only, can be obtained to the same degree when entirely excluding the softer more irritating rays. A lupus therapy on that basis would at any rate meet with many practical difficulties.

Now, as to the results of the radium treatment at Finsen's Light Institute I need only say a few words while referring to the cases stated here. It is beyond doubt that it is possible to obtain healing of the lupus foci and consequently a permanent cure in certain cases of limited extension. Besides the first case, to which radium treatment was exclusively applied, the Cases 2, 4, 5, and 15 show this with regard to some smaller areas. But even if cure has apparently occurred, one should be prepared to see relapses *in loco,* as in the Cases 5 and 15, just as with any other treatment.

In the majority of cases, however, we did not meet with such favourable results. Even if an unquestionable improvement has been demonstrable with some patients, it took a long time before it occurred, or it was followed by retrogression or at any rate absolute stand-still, so that we thought it correct to give up radium for the benefit of light treatment. In fact, by continuing this treatment, with the majority of patients, on other diseased areas we had an excellent control to judge the results. In other cases it did not seem at all possible to show any action, and in a few cases there was an immediate retrogression, such as may occur at the start of any other kind of treatment.

Of course, to be just in one's judgment, one should take into consideration the nature of the disease in question and what is obtainable by other forms of treatment. Lupus vulgaris is, as we know, a disease the prognosis of which should always be formed with some prudence; a great deal depends here on the point of time at which it comes under treatment and on the degree to which it tends to spread. Even an apparently favourable course may be interrupted by transitory or constantly increasing retrogressions. And, apart from quite small relatively early cases, the cure, if obtainable, will, as a rule, take long, and thus will depend on the energy of the patients, and on their willingness as well as their power to carry through the treatment.

In all these different points the conditions, as far as our material was concerned, were quite uniform both with the radium treatment and the Finsen treatment, and over and over again, if not in all cases, we have concluded that it was the *latter that most quickly led to improvement or healing.*

Considering, finally, that the cicatrisation after the radium treatment, much more than after light and even X-ray treatments, even when undertaken with all necessary care, is cosmetically less satisfactory owing to atrophy, depression, and disfiguring telangiectases, it is no wonder that we, as the total result of our experiments, *must consider the radium treatment as inferior to our other means of curing the disease.* By the application of a subsequent Finsen treatment, associated, if necessary, with X-rays and universal arc-light baths, the action of which we in these last few years have learned to value highly, so much is really attained in the shortest time possible that radium as a means of cure in the case of Lupus vulgaris becomes, so to speak, superfluous. In quite special cases at periods of absolute stand-still this means may be worth trying. But often the extension of the disease will then limit its applicability.

THREE CASES OF SO-CALLED MULTIPLE IDIOPATHIC HÆMORRHAGIC SARCOMA (KAPOSI).

BY F. PARKES WEBER, M.A., M.D., F.R.C.P.Lond.

CASE 1.

THE patient, J. Z—, who was born in Galicia in 1856, of Hebrew parents, was shown at the Dermatological Society of London on February 8th, 1905.* At that time the age given was incorrect, but his correct age at present is 60. In 1905 he presented the typical bluish nodules in the skin of the right foot, the left lower extremity, the hands, and the penis. In some of these parts, in addition to the bluish nodules, there were small sessile or pedunculated outgrowths (see Fig. 1). There was also considerable chronic œdema of the left foot and ankle, such as is present in many cases of the disease, especially in one or both of the lower extremities if severely affected.

The illness was said to have commenced about three years previously (about 1902), when he chanced to wound the sole of his right foot with a nail. A pedunculated growth arose from the wound, which was removed by a medical man. Afterwards small, slightly elevated, hard, bluish or purple spots appeared in the skin of the lower extremities, especially the feet, and the left foot and ankle became swollen. From time to time sessile or pedunculated outgrowths, mostly not larger than a lentil or pea, developed on the affected parts, chiefly on the left foot, and the little pendulous tumours tended to become ulcerated, and dropped off or were knocked off accidentally. The disease did not cause any pain or itching to speak of.

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* F. Parkes Weber and P. Daser, *Brit. Journ. Derm.*, 1905, vol. xvii, p. 135. The age given was incorrect. The case was also shown at the Dermatolgical Section of the Royal Society of Medicine on January 20th, 1916 (*Proc.*, 1916, ix. p. 62).

The patient was for a time treated with arsenic, and for a time externally with lead lotion. In June, 1906, there was a temporary erysipelas-like attack in the left lower limb. For the last four years or so he says he has had no treatment at all for the skin-disease in question. At present he is well and active, excepting for some troublesome seborrhœic eczema. There is practically no œdema of either leg. The left lower extremity is still the more affected of the two (see Fig. 2). There are brown-red or purple patches on the feet and (much less) on the legs. On the feet and legs there are a few small dark-coloured, hard cutaneous nodules, and there are a few small lesions on the thighs and elsewhere. There are no longer any of the little pedunculated outgrowths such as he used to have. The practical absence of œdema and the general appearance of the affected portions of the skin prove that the disease has in the main become quiescent and that considerable involution has taken place in the lesions.

The patient seems to have remained free from visceral disease and has never suffered from gout. His Wassermann reaction is negative. There is at present slight enlargement of the inguinal and right axillary lymphatic glands, but this may be connected with the eczema. His father lived to very old age.

Little polypoid outgrowths from the diseased parts were obtained for microscopical examination in 1905 and 1908. They consisted mainly of oval and spindle cells in the corium. These cells were more or less grouped into strands or bundles, and were cut in various directions. In some parts there were empty spaces (lymph-spaces or newly formed blood-channels ?); in some parts there was extravasated blood; in other parts there was a homogeneous substance between the cells indicating œdema. On a specimen examined in 1908* I remarked that the growth in the corium consisted chiefly of spindle-shaped and elongated cells, arranged to some extent in strands and bundles, and richly supplied with capillaries distended with blood.

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* *Proc. Roy. Soc. Med., Clinical Section*, 1908, i, pp. 235, 236.

Besides the dilated blood-vessels there were dilated lymph-spaces in the growth, and in places there was extravasation of blood.

Dr. J. M. H. Macleod made a careful microscopical study of the pieces removed in 1905,[*] and came to the conclusion that the case in question, while presenting the typical clinical characteristics of the affection described first by Kaposi and observed repeatedly since, was histologically "not a sarcoma, but a growth of organising connective-tissue cells associated with marked vascular dilatation, œdema, and the deposition of blood-pigment."

CASE 2.

The patient, G. Z—, aged 77½ years, a Jew from Russian Poland, is a rather corpulent man, of somewhat plethoric appearance.[†] Over his extremities, and to a lesser extent over his face and trunk, are raised spots and plaques of various shapes and sizes, varying in colour from red or purple to brownish-purple. The brown colour (due probably to deposition of hæmosiderin in the skin) is well seen when the blood is squeezed out of the lesions by pressure with a glass lens. The distribution of those spots and plaques is mainly peripheral,[‡] the lesions being actually confluent at the extremities of the limbs, so that both hands and both feet appear uniformly turgid and of a purple colour. The legs, up to the knees, and the forearms are much more affected than the thighs and upper arms. There is chronic œdema (as there often is in one or both lower extremities, if much affected, in these cases) of both legs up to the knees. He has several spots over the buttocks and a few on the abdomen (see Fig. 3).

Scattered over the face are red papules of the same nature, and, owing to the disease, the face has a somewhat turgid "leonine" appearance, at first sight suggesting the possibility of tubercular leprosy.[§] On the glans penis at the urethral orifice is a swollen hypertrophic papule, which is now pale, but is said to have been formerly red, like the other lesions.

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[*] J. M. H. Macleod, *Brit. Journ. Derm.*, 1905, vol. xvii, p. 173.

[†] The patient was shown at the Dermatological Section of the Royal Society of Medicine on July 16th, 1914 (*Proc.*, 1914, vii, p. 288).

[‡] Owing to the peripheral distribution of the main lesions in this disease Unna proposed the following name for it: "Acrosarcoma multiplex cutaneum telangiectodes."

[§] Zambaco Pasha and others at first suspected that Pringle and Stephen Mackenzie's case might be one of leprosy. See the discussion on Schwimmer's paper in the *Trans. of the Third Internat. Cong. of Dermat.*, 1896, p. 261.

On the whole, the lesions are more raised and hypertrophic-looking, and more dusky (from congestion) on the legs than on the arms. Some of the larger plaques are paler and less raised in parts (especially in the central parts) as if fading away there, whereas in other parts (for instance, sometimes on one side) they appear to be still active, as if, in fact, the lesions in question were spreading in one direction and undergoing involution in another. Pruritus is certainly not a troublesome feature; there is slight itching in the cutaneous lesions at times, but never any actual pain. In this case there are none of the little pedunculated, pendulous, berry-like outgrowths which at one time constituted a notable feature of the disease in Case 1. There has been no serious attempt at any special treatment, I believe.

The disease seems to have commenced gradually rather more than four years ago, but during the last two years there has been very little progress or change of any kind. The patient appears to have been a strong man, but he has some chronic bronchitis and is at present rather wheezy. The Wassermann reaction is negative.

Microscopical examination of one of the lesions in this case (see Fig. 4) shows what I take to be a proliferation of fusiform cells and connective-tissue elements in the corium, together with many clefts, which are doubtless, as Dr. J. C. G. Ledingham kindly points out, newly-formed lymph-spaces, or perhaps also blood-channels. By the Unna-Pappenheim stain (methyl-green-pyronin) there seem not to be plasma cells present. The layer immediately below the epidermis is relatively clear (slightly stained) owing to its being œdematous. Dr. Ledingham likens the main change to one that occurs in lymph-angiomatous or hæmo-lymphangiomatous processes. He suggests that the cells permeating the corium are largely of the endothelial type of cells which line the lymph-spaces and blood-spaces in angiomata.

CASE 3.

The patient, M. G—, aged 25½ years, is a well-built man, a tailor, of Hebrew parents, from Russian Poland.* At the age of 1 year he was brought by his parents to England. He has numerous elevated purple (and brownish-purple) nodules and patches of various sizes and outlines in the skin of his left hand and both feet and both legs below the knees. In the lower half of each thigh there are several hard nodules, quite as large as almonds, situated more deeply in the skin than the other lesions. They appear to be separated from the surface (which is not coloured, or is only very slightly purplish) by a layer of normal corium, so that the epidermis is to some extent movable over them.

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* The case was shown at the Dermatological Section of the Royal Society of Medicine, October 19th, 1916.

No other parts are affected, and, excepting for the skin-disease, the patient seems to be healthy. The Wassermann reaction is negative. The central portions of all the larger patches of the disease are browner, less purple, and not so much raised above the general level of the skin as the margins, which are in parts somewhat nodular. The most severe lesions are on the left foot (see Fig. 5), which, together with the lower part of the left leg, is œdematous. (Œdema is frequently associated with the severer lesions in similar cases.) A nodule of the disease on the sole of the left foot and the tense œdema of that part cause the patient occasional pain. The other lesions sometimes give rise to a temporary sensation of itching or slight pain, lasting ten minutes or so at a time. The superficial lymphatic glands, as usual, are not involved. There are several patches of leucodermia on the right side of the thorax, but they are doubtless not in any way connected with the disease under consideration.

The disease commenced in the latter part of 1914, in the neighbourhood of a birth-mark on the third finger of the left hand. About a month later both feet were already affected. An abscess formed in the left leg about March, 1916, which was successfully treated by my colleague, Dr. J. P. zum Busch. He first saw the patient and correctly diagnosed the nature of the skin-disease, and to him I am indebted for the case. In this patient Roentgen-ray treatment is going to be tried under Dr. J. H. Sequeira at the London Hospital.

A "biopsy" examination of the lesions (sections prepared by Dr. Hans Schmidt) shows changes quite characteristic of the disease (see Fig. 6). In the corium at various levels are numerous dilated (doubtless newly-formed) blood-capillaries. In close connection with these dilated blood-vessels are groups of oval or spindle-shaped cells (with large nuclei), often arranged in interlacing bundles, some cut transversely, some longitudinally. These cells are those which have often been regarded as sarcoma-cells, but are probably fibroblasts and connective-tissue cells, and represent a new formation (proliferation) of connective-tissue elements. There are many capillary hæmorrhages, and in various parts there is a good deal of pigment (intracellular and extracellular), which appears to give the Prussian-blue reaction, and is doubtless derived from extravasated blood. There are very few lymphocytes or plasma-cells.

Remarks.

The disease occurs, at all events as seen in England, almost exclusively in males, especially in Jews from Galicia and Poland between the ages of 40 and 50 years. Case 2 seems to have commenced unusually late in life, about the age of 73 years, and Case 3 commenced unusually early, namely, when the patient was 23½ years old. In Case 3 the commencement of the skin lesions in the neighbourhood of a birth-mark should be specially noted, and likewise that the patient was only about 1 year old when he came to England. In Paulin Martin's case (see further on) the patient had lived all his life in England.

A case recently shown by W. K. Sibley * may be compared with Case 3, firstly, because Dr. Sibley's patient was unusually young (only 19 years old), and, secondly, because the disease in both cases was associated with birth-marks (there was an extensive superficial nævus of the right lower extremity in Dr. Sibley's case).

In none of the three cases was there apparently any gout, syphilis, or alcoholism. Of four cases described by J. H. Sequeira † two had actual gout whilst under observation. There was gout in two cases described by Sir Jonathan Hutchinson,‡ and he stated that gout had been present in other cases.

According to the foreign and English accounts, I conclude that the prognosis is probably somewhat better in the patients in England than in those on the Continent. The patients in England do not seem to die from metastases in the mucous membranes and viscera. My Case 1 has now been under observation for 11½ years, and the disease has largely undergone retrogression and involution. In three

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* W. K. Sibley, *Proc. Roy. Soc. Med., Derm. Sec.*, 1916, ix, p. 222. The patient was born in Russian Poland of Hebrew parentage, Dr. Sibley tells me.

† J. H. Sequeira, *Brit. Journ. Derm.*, London, 1913, vol. xxv, pp. 351-357.

‡ Hutchinson, *Arch. of Surg.*, London, vol. v, p. 237, and vol. vi, p. 132.

cases which have been long under Sequeira's observation,* "there has been no reason to consider that the affection has been dangerous to life, and the Galician Jew under Pringle and Stephen Mackenzie lived for many years after one leg had been amputated, and at his death from heart failure, secondary to pulmonary emphysema and bronchitis, the cutaneous affection had disappeared."

On the other hand, of Dalla Favera's six patients † three died. One died from tuberculosis, and in the other two metastases of the skin-disease were found in the viscera. Dalla Favera, however, admitted that the lesions had only a moderate power of extension, and might even resolve and disappear. According to him, the duration of the disease was from two to more than twenty years, the average duration being from eight to ten years.

In regard to the little sessile or pedunculated polypoid tumous that occur in some cases (as in my Case 1), I will recall an interesting example shown by Paulin Martin, ‡ of Abingdon, at the Annual Meeting of the British Medical Association in July, 1904. The patient was a man, aged 75 years, a ropemaker by trade, who had resided in the Vineyard, Abingdon, all his life. In 1894 he first noticed a black spot on his left toe. In three years many more black spots appeared on the soles of both feet, calves, thighs, hands, and arms, but not on his trunk. Currant-shaped "bosses" frequently formed on the black spots. The spots themselves did not disappear, but the projecting bosses occasionally did. Frequently the projections ulcerated, becoming tender for two or more months, and ultimately healing. Pressure applied for a short time would cause ulceration of the projecting bosses, but not of the smooth black spots. Œdema of both legs had been constant for nearly three years.

About the nature of the lesions there has been a good deal written in England and considerably more abroad. Gilchrist and Ketron, in their recent paper on the subject,* conclude that "the lesions begin in the skin as angiomata, due to a proliferation and dilatation of the blood-capillaries, which are very frail at first and liable to rupture. This is followed by a proliferation of the interstitial connective-tissue and endothelium, which gradully obliterates the blood-spaces, forming solid tumours. In the early stages these resemble, in some areas, young connective-tissue, in others areas, sarcomata. As the lesions grow older they assume a more fibrous aspect, and may undergo involution. Coexistent with the formation of the tumours there is a sclerosis of the small arteries supplying them, causing a gradual decrease in the amount of blood. To this is due, most likely, their later evolution as well as involution."

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* J. H. Sequeira, *loc. cit.*

† Dalla Favera, *Arch. für Derm. u. Syph*, 1911, vol. cix., p. 387.

‡ Martin, *Brit. Med. Journ.*, 1904, ii, p. 999. The case was also shown by Sir Jonathan Hutchinson at the Polyclinic, London, in December, 1904, and by J. A. Ormerod, at the Dermatological Society of London, on July 8th, 1903. The fact that the patient had resided all his life in England is specially to be noted. Dr. Martin kindly informs me that the patient died about 1906. For the last five months of his life he was confined to bed and suffered from incessant vomiting. The "black spots" increased and were obvious all over the body, even the tongue and lips being black in places. He was not of Hebrew origin.

Mr. S. G. Shattock, who kindly examined sections from Cases 2 and 3, described in this paper, wrote that in his opinion the condition in Case 3 was best regarded as irritative proliferation of the connective-tissue cells. "They occur in close association with small blood-vessels, the walls of which participate in the proliferation process." He regarded Case 2 as histologically of the same kind.

The fact that the lymphatic glands are usually not affected is a point of some importance.

I think, however, that the balance of evidence from the published literature on the subject points to the disease in question being due to some local microbic infection, the cutaneous lesions representing a tissue-reaction towards the as yet unknown invading microbes. The peculiarity of the tissue-reaction lies in the new formation of dilated capillaries and lymph-spaces and the proliferation of the connective-tissue elements, with usually very little evidence of inflammatory cell-infiltration. It is interesting in this connection that Dalla Favera † pointed out that in several cases the outbreak of the disease had followed on a trauma; and in my Case 1 it apparently commenced from a wound (by a nail) on the sole of one foot.

ILLUSTRATIONS.

Fig. 1.—Photograph from Case 1 (1905).
Fig. 2.—Photograph from Case 1 (1916).
Fig. 3.—Photograph from Case 2 (1914).
Fig. 4.—Microscopical section from Case 2. (× 180).
Fig. 5.—Photograph from Case 3 (1916).
Fig. 6.—Microscopical section from Case 3. (× 180.)

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* T. C. Gilchrist and Ll. W. Ketron, *Journ. Cut. Dis.*, 1916, vol. xxxiv, p. 429.

† Della Favera. *loc. cit.*

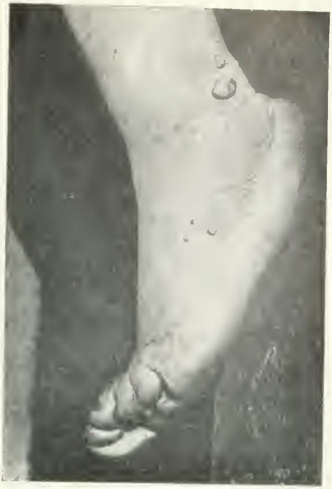

FIG. 1.—Photograph from Case 1 (1905).

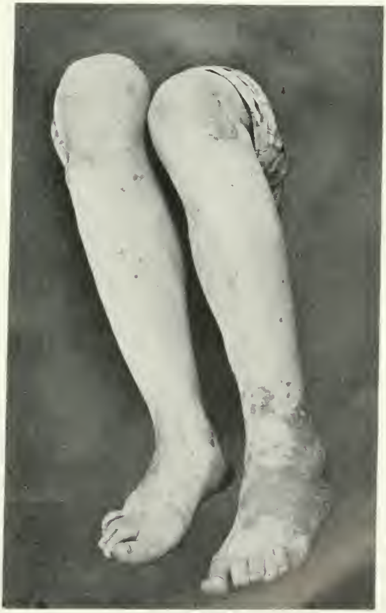

FIG. 2.—Photograph from Case 1 (1916).

TO ILLUSTRATE DR. F. PARKES WEBER'S THREE CASES OF SO-CALLED MULTIPLE IDIOPATHIC HÆMORRHAGIC SARCOMA (KAPOSI).

To face p. 316.

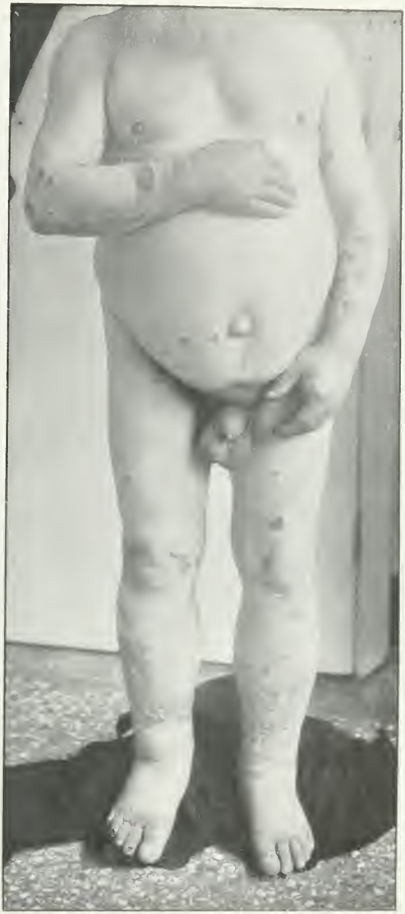

FIG. 3.—Photograph from Case 2 (1914).

TO ILLUSTRATE DR. F. PARKES WEBER'S THREE CASES OF SO-CALLED MULTIPLE IDIOPATHIC HÆMORRHAGIC SARCOMA (KAPOSI).

[*To face p.* 316.

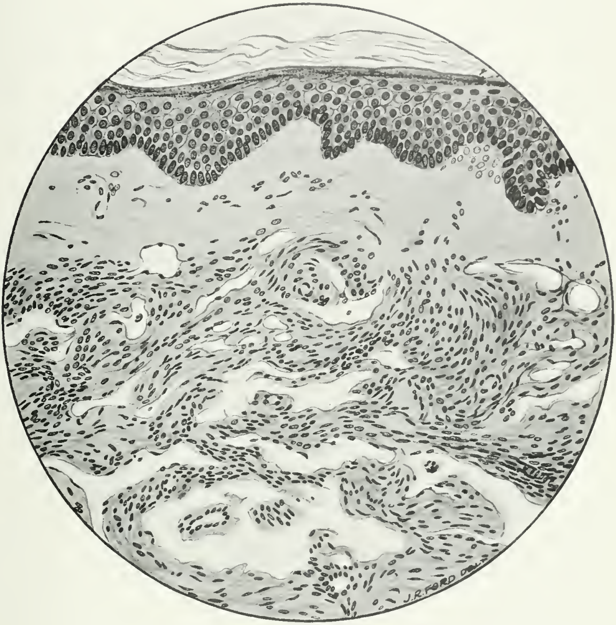

FIG. 4.—Microscopical section from Case 2 (× 180).

TO ILLUSTRATE DR. F. PARKES WEBER'S THREE CASES OF SO-CALLED MULTIPLE IDIOPATHIC HÆMORRHAGIC SARCOMA (KAPOSI).

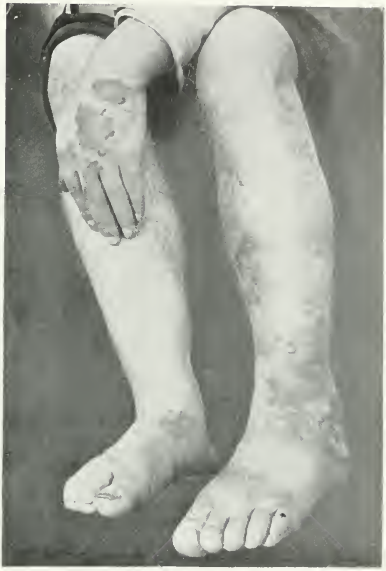

FIG. 5.—Photograph from Case 3 (1916).

TO ILLUSTRATE DR. F. PARKES WEBER'S THREE CASES OF SO-CALLED MULTIPLE IDIOPATHIC HÆMORRHAGIC SARCOMA (KAPOSI).

To face p. 316.

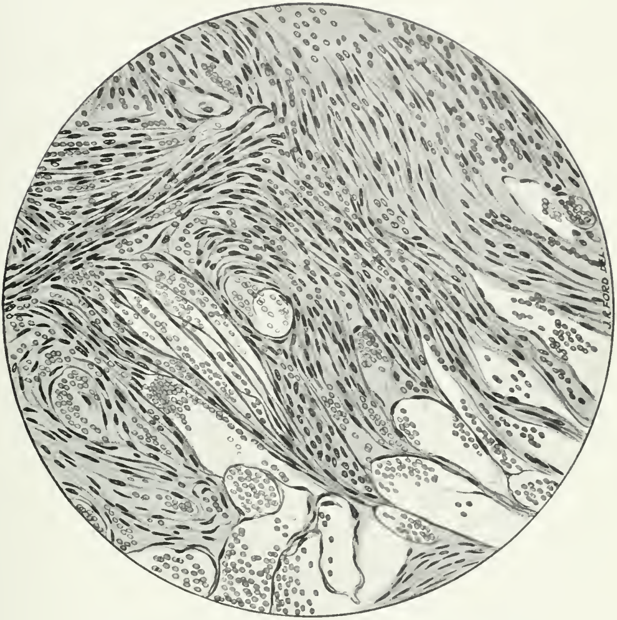

FIG. 6.—Microscopical section from Case 3 (× 180).

TO ILLUSTRATE DR. F. PARKES WEBER'S THREE CASES OF SO-CALLED MULTIPLE IDIOPATHIC HÆMORRHAGIC SARCOMA (KAPOSI).

[*To face p.* 316.

CLINICAL NOTES.

NOTE ON A CASE OF ERYTHEMA SERPENS OF PISCINE ORIGIN.

By GEORGE PERNET, M.D.

Erythema serpens was originally described by Morrant Baker in 1873,* as is well known in England, but somehow or other it has got mixed up with the Erysipeloid of Rosenbach (1897), with which it does not seem quite to fit in. Whether Erysipeloid be the same or an allied condition of higher degree matters not, the name Erythema serpens should be adhered to for the condition described by Baker.

Owing to the close vicinity of the great Smithfield meat market, Morrant Baker had more opportunities of observing the disease among patients at St. Bartholomew's, as is no doubt still the case. Looking through my West London Hospital notes, the case I am about to describe is the first to have presented itself in my clinic during the last three years. Although I have seen a few cases at odd times, this is the first one as far as I recollect to have been connected with dressing fish in my experience. I am quite aware that Gilchrist, of Baltimore, has described a good many instances of the condition due to crustacean crab-bites. Baker refers to sixteen cases originating from bones, dressing suet and "high" game, handling rabbit-skins, a dog-bite, a splinter of wood, cuts from falling, etc., but fish is not mentioned. It is for that reason the following details may be of some interest.

The patient was a woman, aged 25 years, employed as a fish-filleter at a big firm of caterers. She was first seen on July 14th, 1916 (N. 3674). The trouble was of fourteen days' duration, and had followed a slight injury to the left thenar eminence in the course of her work, whence it spread up the wrist like an "erysipelas." This had all subsided except at the seat of the inoculation and about the inner side of the hand from the metacarpo-phalangeal to the metacarpal joint, which presented a slight erysipelas-like blush. Her temperature was 99·6° F. Mist. quin. sulph. and a lactate of lead lotion were ordered. On July 21st there was a faint pink blush about the dorsal aspect of the left middle finger and also about the terminal phalanx of the left little finger, the original erythema having disappeared. The erythema was very like the pink blush depicted in Baker's plate. In this case the erythema jumped from one point to the other as insisted on Baker in his original description, so that the Erythema is not only *serpens* *saltans* as well.

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* *St. Bartholomew's Hospital Reports,* vol. ix, 1873, p. 198 (with coloured plate).

TWO CASES OF ACUTE STREPTOCOCCAL NECROSIS OF THE SKIN AND SUBCUTANEOUS TISSUES.

By HENRY MacCORMAC, M.B., M.R.C.P.

In the two cases to be described the destruction was extensive and appeared to result from a local streptococcal infection. Both have certain features in common, insomuch that it was possible to correctly foretell the casual organism in the second from observation of the first.

Case 1.—Admitted to hospital on January 4th, 1915. G. R—, female, aged 38 years, married.

Previous history good; pregnant on admission into hospital. During each of five previous pregnancies a varicose condition of the veins of the lower extremities had been noted. The disease began with the appearance of several large blebs on the skin over the inner and front aspects of the lower half of the right leg. Within twenty-four hours these had ruptured, and soon afterwards there appeared an ulceration of the underlying structures. This ulceration progressed with an astounding rapidity, so that in a few days a deep excavation had resulted. At this stage, when the patient was admitted to hospital, the right leg and foot were greatly swollen and œdematous; there was a deep ulceration of the inner and anterior aspects of the lower half of the right leg and foot, extending below the internal malleolus. The margins, rather "punched out," were irregular in design; the base was covered with a tenacious yellowish-brown slough. A bright erythematous blush, fading into the normal skin, surrounded this excavation.

During the next few days the ulceration became progressively deeper, so that the more resistant anatomical structures (tendons, veins, etc.) were laid bare.

Progress.—January 28th: *B. pyocyaneus* found in pus. Wassermann test negative.

February 3rd: Two new abscesses formed in neighbourhood of large ulcer. From these a streptococcus and *Staphylococcus aureus* were cultivated.

March 13th: Patient discharged with wound healing by granluation.

Treatment.—A mixed streptococcal and staphylococcal vaccine (autogenous) was administered in doses of 20 million streptococci and 60 million staphylococci. The leg during the more acute period was continuously immersed in boric lotion.

It may be observed that the temperature during the whole period was of moderate degree, falling to normal by the fourth day after admission, except for a reaction on March 3rd after an administration of vaccine.

Case 2.—Admitted into General Hospital on February 10th, 1916. Private H—, R.A.M.C., aged 21 years.

About ten days before admission (*i.e.* February 1st) a swelling was noticed over the upper sternal region; this increased rapidly in size and was extremely painful. It was incised on February 3rd and pus evacuated.

February 10th (admitted into General Hospital): The patient was obviously ill; there was an oval excavation, some 1½ inches long, over the right side of the manubrium sterni. Surrounding this for a distance of some two inches there was a tender and swollen erythematous area. A probe could be passed vertically down for one inch to bare bone; pus was discharging freely.

February 14th. Operation: The wound was enlarged and necrosed portions of the manubrium sterni removed. Behind this pus was found, from which streptococci in pure culture were obtained.

After this the patient made an uninterrupted recovery, and was discharged convalescent on March 8th, 1916.

These two cases are instances of an unusual reaction to streptococcal infection. In both the onset was acute; in both, in an unusually short space of time, extensive and deep destruction of tissue occurred. It is difficult to realise how rapidly this process took place, the alteration in the first case from a comparatively superficial abrasion to a deep sloughing ulceration occurring in some three days.

It may be assumed that the causal organism in both cases was a streptococcus; the initial bullæ in Case 1 was in itself evidence of this; pyocyaneus and staphylococci were probably secondary, and possibly unimportant, infections. In Case 2 only streptococci were found.

In both cases the disease originated on and in otherwise healthy skin.

The most striking features were the rapidity of destruction of tissue and the depth to which the process extended.

I have to acknowledge the kindness of Dr. Pringle, under whose care patient No. 1 came, and Capt. Every-Clayton, R.A.M.C., who has permitted me to use his notes of case No. 2.

OBITUARY.

ALBERT NEISSER (1854–1916).

By the death of Albert Neisser Germany has lost one of her most distinguished dermatologists. He was Professor of Skin and Venereal Diseases in Breslau University, and chief of the large department for these diseases there. Ever since the age of 25, when Neisser discovered the gonococcus, his name has been associated with work on many branches of his subject.

He owed much of his success to the fact that he took a wide view of his subject, and his work was based on a good knowledge of general pathology and bacteriology. In his laboratory he did not confine himself strictly to dermatology. He directed research in general histology, bacteriology, protozoology, X-rays, Finsen light, etc. He spent many years on important work on syphilis. He had a large monkey-house in his private garden and often had over two hundred monkeys there for experimental work on syphilis. He spared no trouble nor expense. As the animals did not thrive well in Germany he equipped and maintained an expedition to Batavia, where he and his assistants did research work on syphilis in monkeys in their native country. Much of this work did not lead to practical results, but to Neisser we owe a great deal of our knowledge of immunity to syphilis. He was quick to take up new ideas and to recognise the work of others. I remember well how, when Schaudinn discovered the spirochæta pallida, Neisser at once started to confirm the work. Later he was associated with Wassermann and others in working out the reaction which goes by Wassermann's name. He was a strong enough man to admit when he was wrong, and to change his views as he did in regard to Molluscum contagiosum. He brought the teaching of dermatology in Breslau to a high level. He was a good speaker and a very enthusiastic teacher. Men came from all parts of Germany and from other countries to study under him. Many of his former assistants are now occupants of chairs of dermatology in Germany, Austria, and Switzerland. His department was thoroughly equipped with laboratories, a large museum of models of skin and venereal diseases, a complete electrical department with X-rays, Finsen light, etc., and a good library.

Neisser had a very extensive knowledge of the literature of his subject, and the *Arvhiv. für Dermatologie* was under his immediate control for many years. He was also closely associated with the publication of the *Ikonographia Dermatologica.* In addition to his many other activities he had an extensive private practice. As a man he was respected by his colleagues, and his opinion always carried weight. He was fond of music and art. His beautiful house on the outskirts of the city, with its wonderful mural paintings and decorations, is one of the finest in Germany. He leaves a widow and an adopted son.

R. C. L.

ROYAL SOCIETY OF MEDICINE.

DERMATOLOGICAL SECTION.

MEETING held July 20th, 1916, Dr. J. H. STOWERS, President of the Section, in the Chair.

Dr. E. G. GRAHAM LITTLE showed a case of *Xanthoma tuberosum.* The patient was an Irish lady, aged 50 years, living near Dublin, Ten years ago a swelling began to appear in the fleshy part of the right upper arm above the elbow. It was painless and gave no discomfort, but increased slowly in size, and there was now a tumour, about $\frac{3}{4}$ in. in diameter, freely movable with the skin, to which it was firmly attached, and in which it appeared to sink to the depth of about $\frac{1}{2}$ in. This was probably also xanthomatous, but the colour was a much fainter yellow than the other lesions about to be described. Two years ago small lemon-yellow nodules began to appear on the backs of both elbows, where there was now an eruption of closely aggregated typical xanthomatous tumours, from $\frac{1}{4}$ in. to $\frac{1}{8}$ in. in diameter, raised to about the same degree above the level of the surrounding skin, quite painless, and indeed giving rise to no subjective sensations, but spreading in extent so that the backs of the elbows were quite covered with eruption. More recently similar nodules had broken out on the front of the knees, where they were still very few in number, and on the skin over the lower sacral region. There was nothing in the mouth. The furrows of the palm of the hand were slightly yellower than the normal skin, and probably there was an early xanthomatous change there. With this exception the skin was everywhere else normal. The urine had been examined for sugar and acetone, neither of which was present. There was no history of diabetic inheritance and the patient enjoyed excellent health. She had never been pregnant and had been married twenty years. She still menstruated normally. Whilst in Ireland she had had two applications of X-rays to the elbows, without any effect on the nodules.

In its distribution and general characters the case reminded him strongly of a patient, a London surgeon, shown by Mr. Willmott Evans to the Dermatological Society of London in 1902.* In that patient the eruption disappeared after some applications of X-rays, but he understood reappeared in the same positions shortly after, and although at the time of showing there was no evidence of diabetes, he died of that disease some seven years later. In a case of very remarkable xanthomatous tumours on the hands and feet in a girl, aged 6 years, brought by him before the International Congress in 1913, in whom the diagnosis was confirmed by histological data, there was a family history of diabetes, but the patient herself showed no symptoms of weakened sugar tolerance after several tests, and there was no glycosuria or acetonuria. In this case freezing with carbon dioxide effected considerable, but he understood only temporary, improvement. X-rays, which were given a prolonged trial, had no effect. A coloured photograph and description of this case was contributed by him to the *Medical Annual* for 1915, p. 679.

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* *Brit. Journ. Derm.*. 1902, xiv, p. 465.

He believed there was good reason to regard Xanthoma planum as of different nature to Xanthoma tuberosum, but that this disease and the so-called Xanthoma diabeticorum were essentially the same affection. The development of Xanthoma tuberosum should thus be considered as a possible forerunner of diabetes, and frequent examinations of the urine should be made throughout such a case, and the diet should be regulated so as to throw as little strain as possible on the patient with regard to the elimination of sugar. He confessed he was sceptical of any advantage to be derived from local treatment short of excision of the developed nodule. As the condition was usually troublesome only because of the disfigurement, treatment was relatively unimportant as compared with the attempts at prevention of the development of diabetes.

Dr. G. **Pernet** remembered the condition in the surgeon cleared up wonderfully under the X-rays.

Dr. **MacLeod** thought that members would perhaps recollect a most remarkable case of this disease which he showed several times at the Dermatological Society of London and also at the last International Congress of Medicine. The patient was a man with a more extensive xanthoma than he had ever seen or read of in any other case. He had had him under observation during the last six years and had had ample opportunity of trying all manner of local treatments. So far the results had been most disappointing; he thought there was some improvement following X-rays, but relapse occurred afterwards. Carbon dioxide snow gave equally unsatisfactory results, and finally he had abandoned local treatment. What had interested him most in the case was that, in spite of the ever increasing deposition of fat in the skin and other tissues, he had been able to detect nothing abnormal either in the blood or urine. Dr. Topley, of Charing Cross Hospital, kindly investigated the blood for him from every point of view of which he could think, but was unable to detect any definite abnormality.

Dr. **Pringle** stated that the lesions sometimes involved the arteries; he remembered seeing an aorta studded with them.

Dr. J. H. **Stowers** (*President*) showed a case of *tuberculous disease of the face of five years' duration in a girl aged* 18½ *years*. This was an unusual case of so-called "Lupus vulgaris." The disease commenced in the mouth about the left angle, and developed into a superficial irregular erosion, with ulceration of the mucous membrane of the lip and gums. Typical lupus nodules appeared on the skin below the left angle of the mouth, and a well-defined patch upon the chin. Well-marked enlargement of the glands on both sides of the neck below the rami of the jaw and around the carotid vessels on both sides existed. Much of the disease disappeared under treatment both general and local. The nose and throat were unaffected.

In 1914 fresh nodules on the gums appeared, and still existed in spite of remedies.

He was exhibiting her on account of the large mass of tuberculous tissue which now involves the right cheek. The infiltration, which was ½ in. in thickness and was of rounded form and 1½ in. in diameter, was gradually increasing. In spite of very numerous applications both of X-ray and Finsen light, extending over a period of eighteen months, no satisfactory result had been obtained.

He would be glad to hear any suggestions from members as to appropriate treatment. He might add that the general health of the patient was satisfactory.

Dr. PERNET asked if iodide of potassium and chlorine water had been tried in the case.

Dr. A. EDDOWES suggested that the infiltrated tissue should be injected with a non-irritating preparation of mercury. He had already mentioned to the Section a case of his, a man, in whom a large mass of tuberculous tissue occupied the whole of one side of the buttock. He injected the mass, in three different sections, with various preparations of mercury. Eighteen months afterwards he was amazed to find the infiltration gone, and he did not know which mercurial preparation did most good. He had several patches of lupus about him, and he amputated a piece of one of his ears for the condition. The buttock patch, however, was too large for excision. He also thought this girl's case was one *par excellence* for the internal administration of arsenic.

Dr. KNOWSLEY SIBLEY presumed iodide of potassium and chlorine water had been administered. He suggested that he should try dusting or blowing on to the areas of ulceration in the mouth a powder consisting of equal parts of iodide of potassium and chalk, and afterwards get her to hold her mouth full of chlorine water as long as she could. He had had some cases which had done extremely well on that treatment. And he would continue the internal use of iodide of potassium and chlorine water.

Dr. R. PRICHARD asked if an ointment of biniodide of mercury, 4 gr. to the ounce, had been used. It had a very good, penetrating effect.

The PRESIDENT (in reply) stated that Pfannenstiel's treatment was adopted in the earlier stage without success, and the only other local applications had been carbolic acid, chromic acid, the acid nitrate of mercury, oleate of mercury, and a pyrogallic acid ointment. General tonics, including iodide of iron, and cod-liver oil with malt, had been administered.

Dr. GEORGE PERNET showed a case of *Dermatitis herpetiformis in a boy*. The lad, aged 9 years, was first seen by him on February 18th, 1916, when the following notes were made: "Duration, sixteen months. Began with redness followed by blisters. The lower part of the neck and clavicular regions are reddened with vesicles here and there. In the region of the umbilicus, the lower part of the abdomen, and upper part of the thighs, there are erythematous areas with a number of vesicles scattered about on them, also bullæ ¼ in. in diameter; on the back of the neck a group of subsidiary vesicles; centre of back and about buttocks subsidiary erythema. Patient gets quite clear at times, but fresh attacks occur." The patient had had a variety of treatment, *intra and extra*. He recommended a trial of salicin internally, and lotio calaminæ. He saw the patient two or three times, but owing to a rigor, and a temperature of 104° F., he was prevented attending as arranged, and he had not seen him since until the present moment. Now he had a very severe attack which started a month ago after an interval of freedom of three weeks, so he was informed. At the moment the upper part of the chest and abdominal region in front were covered by erythema, vesicles, and large bullæ, in various stages of development and involution; at the back the eruption was less in degree. No itching was complained of, but pain. This brought the case into the category of Brocq's *Dermatites polymorphes douloureuses aiguës récidivantes*. The difficulties in the way of treatment in these cases were well known.

Mr. SAMUEL suggested that this was not a case of Dermatitis herpetiformis, but one of Pemphigus, and for the following reasons: The lesions started as blisters pure and simple on apparently normal skin. He had inquired most carefully into that point, and the present amount of erythema was all subsequent and not antecedent to the bullæ, which was strong evidence against the diagnosis of Dermatitis herpetiformis and in favour of Pemphigus. Again, the child did not complain of itching, but only of soreness, which was what one expected in Pemphigus as against Dermatitis herpetiformis. Dermatitis herpetiformis must be extremely rare in children. Another point against the diagnosis of Dermatitis herptiformis was the fact that the child had been definitely ill, which was not a feature in that disease except as a result of insomnia due to intolerable itching (which was absent in the present case). Therefore he thought that they would entitle this case Pemphigus in a boy.

Dr. GRAHAM LITTLE remarked that they had a similar discussion on terminology on the same case when he showed it there, eight or nine months ago, as Dermatitis herpetiformis, which was his preference of the two names in a condition where there was considerable itching, as there then was, and very scanty eruption. At that time he did exceedingly well on arsenic; the benefit was almost instantaneous. He did not know whether he had had any lately.

Dr. PERNET, in reply, said the lad was not now under his care; he was in the Kensington Infirmary under Dr. Potter. When the boy came to the West London Hospital he had distinct erythematous patches, and on some of them were vesicles and bullæ; some of them were grouped. That attack was not such a severe one as the present outbreak. It was well known that Kohn-Kaposi never admitted there was such a condition as Dermatitis herpetiformis; he said that what went under that name was Pemphigus. But there was no doubt there was a Dermatitis herptiformis type of vesiculo-bullous eruption associated with erythematous patches, and this case was of that kind. These lesions were very painful; and that brought it into the Brocq category of the *Dermatitis polymorphes douloureuses récidivantes.* Itching might be absent in children, as in a typical case which followed varicella that he saw with Radcliffe-Crocker. Certain vesiculo-bullous eruptions were related to one another, but, for purposes of diagnosis, they put forms like the present into the Dermatitis herpetiformis group. He agreed that arsenic might be of service there. That he had already had. He recommended the trial of salicin.

Dr. GEORGE PERNET showed a case of *extensive exuberant Lupus vulgaris of the leg originating from a tuberculous abscess.* The patient was a girl, aged 15 years. The disease dated from the age of 3, and followed an abscess of the left thigh which was, no doubt, tuberculous. The depressed scar of this abscess was in the middle of an irregularly rounded patch of lupus some 6 in. across, and which was well raised above the level of the skin, especially at the lower border. On the outer and posterior part of the left leg there was a large elongated oval patch of lupus, the long axis being vertical. Although the disease had been slowly extending for twelve years there had been no treatment apart from ointments. The upper patch was the first, and this was followed four months later by the lower focus of disease. The patient was of the fair ethereal type so prone to tuberculous infections.

Dr. GEORGE PERNET showed a case of *multiform Lupus vulgaris following measles, with spontaneous involution of some of the lesions.* The patient was a girl, aged 8 years. The Lupus vulgaris foci followed measles and came out together. Now there were three typical small Lupus vulgaris areas on the left cheek, the lowest one of which had discharged up to six or seven months ago. On the same cheek and above the foregoing lesions there was a small scar. On the right cheek there were several small depressed scars of similar lesions, according to the mother's statement. There was also a small scar on the left calf $\frac{1}{4}$ in. in diameter, and another, rather oval, $\frac{1}{2}$ in. by $\frac{1}{3}$ in., low down on the right calf, the long axis being vertical. The child suffered from chilblains. No history of phthisis could be gathered from the mother, but the fair, blue-eyed type of the patient was that of one prone to tuberculous disorders.

Dr. W. Knowsley Sibley showed a case of (?) *Urticaria pigmentosa in a soldier, aged* 19 *years.* He had an eruption over his trunk, arms, and thighs. It came out suddenly two months ago, and was in the same condition now as then. He had not been taking medicine. The skin was slightly urticarial, but not markedly so. It did not itch, and there were no lesions in the mouth.

Dr. E. G. Graham Little showed a case of *Urticaria pigmentosa in an adult.* The patient, a man, aged 35 years, was sent to him by a Medical Board to ascertain whether he was fit for enlistment in the Army. He was otherwise a robust fellow, suffering little discomfort from his eruption. This appeared apparently acutely at the age of 17 years, and had persisted unchanged ever since. It consisted of small red and reddish brown stains thickly distributed over the wrists, forearms, and arms, and much less extensively on the trunk, both back and front. The face was quite free. The macules were about $\frac{1}{4}$ in. in diameter, and became turgid and vividly red on rubbing; there was considerable factitious urticaria, but very little spontaneous itching.

He had advised the Medical Board that the man should not be accepted for military service. He thought his experience was that of most of them—namely, that these cases were invariably mistaken for syphilis by the general practitioner and still more by the layman, and as the man was very averse to military service he would almost certainly find means to aggravate his eruption, and perhaps still more certainly meet with a medical officer who would regard the rash as syphilitic, not to speak of the disquiet which his eruption would cause his room mates.

Histological examination.—A portion of skin was removed from the upper arm. The section, stained in the ordinary manner with hæmatoxylin and eosin, showed little abnormality. Stained, however, with polychrome methylene blue, and washed with glycerine ether until almost all the stain was removed, the section was typical of Urticaria pigmentosa. The deposit of pigment in the basal layers of the rete was pronounced, but irregular in degree; in some parts of the diseased area the deposit was several layers thick, in others almost absent. The other characteristic feature of the histology of this disease, the enormous increase in mast cells, was much more noticeable and regular, the vessels of the papillary body and of the subpapillary plexus being richly surrounded with mast cells.

Dr. **Graham Little** regarded Dr. Sibley's case as undoubtedly one of Urticaria pigmentosa. The absence or moderate degree of itching was in his opinion no objection to making that diagnosis. In 1905 he collected cases and wrote a paper on this subject, in which after an analysis of the then published cases, he wrote: "It will be seen that in a very large proportion of cases the itching was either very moderate in degree or entirely absent. I am satisfied that *severe* itching must be regarded as a very rare symptom." It was certainly a remarkable circumstance that the Section should have two cases presented on the same afternoon of adult Urticaria pigmentosa, for in the series of 142 cases of the disease collected by him in the paper referred to only fourteen generally accepted cases occurring in adults were found.

Dr. **Pringle** thought there could be little, if any, doubt as to the nature of Dr. Little's case. But in regard to Dr. Sibley's he admitted there were many links of evidence wanting. There had been no antecedent urticarial condition, the eruption did not itch, and the patient had not got an appreciably urticarial skin. His first impression was, and remained, that it was probably an adult case of Urticaria pigmentosa, but he was not certain that it might not be an example of the still rarer condition described by Jacquet and Darier, about thirty years ago,* under the name of "Hidradénomes éruptifs," a condition which appeared suddenly, unattended by subjective symptoms of any sort. None of Jacquet's cases were anything like so extensive as this, but he did not think the mere question of extent ought to decide the diagnosis. He had seen one or two cases of Jacquet's disease in this country, in which it was confined to the chest. He thought a microscopical examination would settle the diagnosis one way or the other.

Dr. **Adamson** regarded Dr. Little's case and Dr. Sibley's case as examples of a not very uncommon type of Urticaria pigmentosa of adults. He showed a case of this sort at a meeting of this Section in February, 1914, and a photograph was published in the *Proceedings* of this Section.[*] He then mentioned five other cases which had come under his care, and recalled a similar case which had been shown by Dr. Douglas Heath.[†] It was characteristic of these cases that there were numerous generalised freckle-like pigmentary macules, which were often mistaken for a secondary syphilitic eruption. Urticaria and itching might be pronounced, or it might be but little marked, or even absent. It might be easy or difficult to produce swelling of the patches by friction. Cases varied much in respect to the urticarial element. Dr. Whitfield had expressed the opinion that this eruption was an independent disease, but Dubreuilh, who had recorded a few examples, regarded them as an adult form of Urticaria pigmentosa.

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* *Annales de Derm.*, 1887, p. 317.

The PRESIDENT said that there were minor differences between the two cases but he regarded them as instances of the same disease.

Dr. A. EDDOWES confirmed what Dr. Adamson said about the behaviour of these cases. Sometimes the urticarial symptoms were hardly perceptible. A fortnight ago he saw a girl with the condition who exhibited marked graphodermia. He rubbed one of the pigmented patches on her back, and in a few seconds afterwards urticarial lesions formed in a group. A week after treatment there was scarcely any urticarial tendency left and the pigmented lesions were obviously fading.

Dr. SIBLEY (in reply) said that there was a slight urticaria in his case, and scratching brought out the lesions more obviously. He had seen on and off for some years a marked case of Urticaria pigmentosa in a man aged 26 years, which had been present for twelve years, and whose skin had never shown any signs of urticaria. The eruption had not changed for years, notwithstanding numerous treatments, and had never given rise to any symptoms.

Dr. W. KNOWSLEY SIBLEY showed a case of *Lichen obtusus corneus*. The patient, A. T—, was a fairly healthy-looking man, a tailor by occupation, aged 32 years. The patient's father was a Russian who was brought to England as a child. His mother was English and was born in London. Both parents were stated to have died from diabetes at about the age of 57 years. Patient was in bed with rheumatic fever for one week ten years ago, the knee and ankles being affected. He had rheumatic pains in these joints from time to time. The lesions of which he complained first appeared on the dorsum of the right hand some twelve years ago, and had gradually increased in number ever since, next appearing on the right forearm, then on the corresponding side of the left hand and forearm. Later on they appeared about the ankles and then over the knees.

There were numerous discrete, disseminated, whitish, dry, hard, round, dome-shaped nodules, almost cartilaginous in consistence, some fifty in number, scattered on the dorsum of the hands and extensor surfaces of the forearms, knees, feet and ankles, completely absent from the trunk. They were sharply circumscribed and discretely arranged. They were of fairly uniform size, about that of a large pea. The intervening skin appeared to be normal. In no place was there any tendency for a coalescence of the lesions. The lesions were always extremely irritable, and the tops of all had been torn off by scratching and exhibited crateriform depression, sometimes filled with hæmorrhagic plugs. Otherwise the skin over the tumours appeared more or less normal, both in colour and consistence. There was some increase in hair growth over and immediately around many of the older lesions. This might be due to the stimulation from local applications. A few small Lichen planus papules were to be seen on the extensor surface of the left forearm just below the elbow. No obvious lesions were present in the mouth. There were also some curious circular and circinate, slightly raised, beaded, lichenoid-like lesions on the penis and scrotum, stated to be scars left from boils. These were not at all irritable, and never had been.

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[*] *Proceedings*, 1914, vii, p. 104.

[†] *Brit. Journ. Derm.*, 1913, p. 410.

The patient stated that sometimes the lesions had disappeared spontaneously, and that he was sure there was some improvement since he gave him a carbolic acid ointment, which relieved the violent irritation, and that one or two small lesions which at the time, now some six weeks ago, were just appearing, had now practically disappeared.

A section taken from a small tumour on the left hand showed the following histological features: The chief changes seen in the section consisted in the marked hyperkeratosis of the stratum corneum, which was excessively increased by the number of its cells, and was transformed into a hard, horny mass. At the base of this layer there were two small cavities which contained polymorphonuclear leucocytes. The stratum granulosum, in places where it was visible, showed a marked cellular increase. There was also a marked increase of the stratum mucosum and the papillæ were increased in length; some of the cells in this layer appeared to be undergoing hyaline degeneration. In the small portion of the dermis which was visible there appeared to be an increase of the connective tissue and of the spindle-shaped cells. There was a dilatation of the papillary and other blood-vessels.

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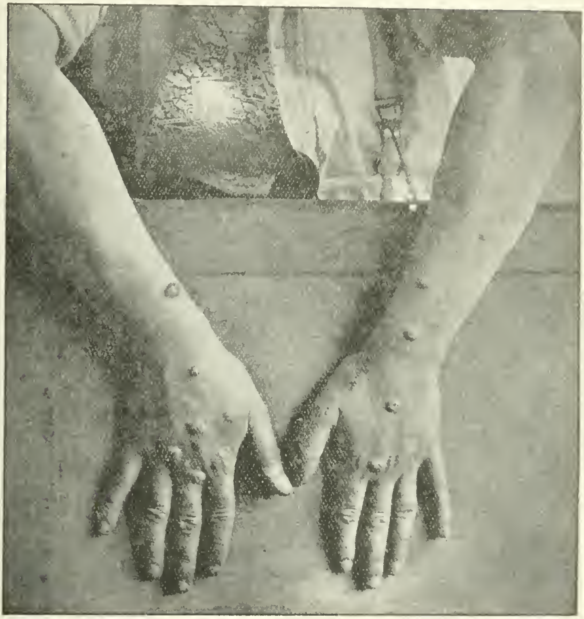

Case of *Lichen obtusus corneus.*

KREIBICH.—*Archiv f. Derm.*, 1899, xlviii.
SCHAMBERG und HIRSCHLER.—*Journ. Cut. Dis.*. 1906, p. 151.
WHITE.—*Journ. Cut. Dis.*, 1907, pp. 216, 217, 385.
ZIESLER.—*Journ. Cut. Dis.*, 1912.

Dr. GRAHAM LITTLE thought this was a clinical variety of hypertrophic Lichen planus. It had a certain resemblance to Granuloma annulare, and in fact strongly resembled an instance which he included in his paper on Granuloma annulare as a possible example of that disease, but more probably of a Lichen planus. The patient was under the care of Dr. MacLeod, who kindly lent him a photograph which was reproduced in that paper.

Dr. MacLeod did not think there was any doubt about the Lichen planus part of this case. He did not think it was the same condition as in the man referred to by Dr. Little, the photograph of whose case did not give a very good idea of it.

Dr. Adamson said that the case shown by Dr. Sibley was undoubtedly an example of the eruption to which Unna drew attention after studying a model in the St. Louis Museum, labelled Lichen obtusus, which Brocq afterwards named Lichen obtusus corneus. In the *Journal of Cutaneous Diseases*,* there was a reproduction of a photograph of a case published by C. J. White, and they would see at once that Dr. Sibley's case presented the same eruption. Lichen obtusus corneus had been usually regarded as a variety of Lichen planus and the presence of typical Lichen planus lesions in the case now exhibited confirmed this view. He believed this to be the first example of Lichen obtusus corneus shown at a meeting of this Section, so that it was evidently a rare form of eruption.

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* "Lichen Obtusus Corneus—An Unusual Type of Lichenification," Charles J. White, *Journ. Cut. Dis.*, 1907, xxv, p. 383; see also "Two Cases of Multiple Tumours of the Skin in Negroes, Associated with Itching," T. F. Schamberg and R. Hirschler, *Journ. Cut. Dis.*, 1906, xxiv, p. 151.

Dr. W. **Knowsley Sibley** showed a case of *Kaposi's multiple pigmentary sarcoma.* S. S—, Russian recruit, aged 19 years, single, barber. Duration of disease: Eleven months ulceration of leg. Clinical features: Deeply pigmented and indurated condition of the right leg with superficial ulceration in places. The whole limb was larger and longer than the opposite side, bone, muscle, etc. The following were the measurements of the right and left legs:

	Right.	Left.
Anterior superior spine to adductor tubercle	20 in.	19 in.
Tubercle of tibia to interior malleolus	15 ,,	14 ,,
Level of tubercle of tibia	$13\frac{3}{4}$,,	$11\frac{1}{2}$,,
Knee-joint circumference	15 ,,	$13\frac{1}{2}$,,
Whole anterior superior spine to interior malleolus	38 ,,	$35\frac{1}{2}$,,

The left leg was normal. There was an extensive superficial nævus of thigh and upper leg.

Histological report of a section taken from a small pigmented patch on the right leg: There was a slight increase in all the layers of the epidermis, and in some parts of the basal layer pigment could be seen. Cellular infiltration was chiefly confined to the upper part of the dermis, and here the pigment was seen to be extracellular. There appeared to be quite an increase in the number of newly-formed blood-vessels, which were also dilated. The Wassermann reaction was negative. The von Pirquet reaction was slightly positive.

Dr. F. **Parkes Weber** remarked that in this case some of the dark cutaneous patch on the right lower limb apparently dated from birth. Although he considered it a typical case of so-called multiple hæmorrhagic (pigment) sarcoma of Kaposi, that was to say typical from the macroscopic point of view, he thought the latter disease was not yet acknowledged to occur congenitally. As, however, he had recently had the opportunity of seeing an absolutely typical case, in which some of the lesions had, according to the patient's mother, been there from one year of age, he thought that he was in a position to assert that (contrary to the accepted opinion) Kaposi's so-called multiple hæmorrhagic (pigment) sarcoma might in rare instances commence early in life, or might be (partly) even congenital. That disease was a non-symmetrical disease, and therefore might sometimes probably be at first unilateral, as in the present patient. As in the present patient, moreover, the disease he referred to was usually accompanied by more or less swelling of the affected part.

Dr. PERNET thought that Kaposi's disease, so-called, was not unilateral.

Dr. S. E. DORE did not think this was a case of Kaposi's sarcoma. It was probably a lymphangioma, and there was no reason why the ulceration and the pigmentation should not be due to the same cause.

The PRESIDENT did not think the nature of this case could be determined without a biopsy.

Dr. PARKES WEBER thought that a biopsy would perhaps help in settling the question of diagnosis. If the cure was really one of Kaposi's so-called multiple hæmorrhagic (pigment) sarcoma, the patient would have a chance of living to old age, since the disease was probably not really a sarcoma, and since other patients with the same disease had, he believed, attained old age.*

MEETING held October 18th, 1916, Dr. J. H. STOWERS, President of the Section, in the Chair.

Dr. H. BATTY SHAW and Dr. D. LOUGHLIN showed a case of *Leucocythæmia cutis.*

(A full description of this case will be published in a subsequent number of the Journal.)

Dr. H. G. ADAMSON showed a case of *Schamberg's disease.* He said that in the *British Journal of Dermatology*, xiii, 1901, p. 1, Schamberg described a case of "Peculiar Progressive Pigmentary Disease of the Skin." The complaint had since been called "Schamberg's disease" by Colcott Fox, Graham Little, and Whitfield, who had shown similar cases at meetings of the Dermatological Section. The characteristic features of the disease were the appearance, particularly on the legs below the knees and sometimes on the arms or wrists, of groups of small reddish-brown spots or points which tended to coalesce to form brownish macules or patches. The eruption was slowly progressive during many years. Subjective symptoms were absent or insignificant. As to the real nature of the disease, or even as to the exact anatomico-pathological conditions which gave rise to the naked-eye appearances, there was no general agreement. The ages of the patients when they first came under observation were 15, 17, 22, 11, and 56 years. All had been males. All observers had descibed the affection as yellowish-brown or brownish patches or macules with outlying red, or reddish-brown, or cayenne-pepper-like punctæ, and earlier groups of isolated punctæ coalescing to form macules. Some had regarded the punctæ as telangiectatic points, others had described them as pigmentary deposits. Whitfield went so far as to say that Schamberg's disease and Hutchinson's Angioma serpiginosum were varieties of the same affection, but Schamberg, though pointing out the resemblance between these complaints, said very truly that the histological picture was different.

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* *Cf.* the case of a patient, aged 59 years, shown by Dr. Weber at the Dermatological Section on January 20th, 1916 (*Proceedings*, 1916, ix. p. 62).

The patient he now brought forward was a man, aged 33 years, who was sent to the clinic at St. Bartholomew's Hospital by Dr. J. Ferguson Weir. The affection first appeared on the right leg four years ago as a group of reddish-brown points, which had since run together into a brownish patch. A little later similar punctæ appeared on the left leg, and while the patch on the right leg had only slightly enlarged, the punctæ and macules had spread over the greater part of the front of the left leg from the knee to the ankle, so that there were now numerous pinhead-sized reddish-brown points scattered and in groups, with amongst them several sixpenny-piece to shilling-sized brownish macules. The punctæ appeared to surround hair follicles. They did not fade on pressure, and they scaled slightly on scaping them. The macules presented the appearance of slight atrophy of the skin. Neither the punctæ nor the macules faded on pressure. There were no subjective sensations. The patient stood for long at a time and there were well marked varicose veins on each leg. Extensively over the right thigh and leg was a deep-purple port-wine nævus which had been present since birth and which was quite different in colour and appearance from the bright brownish punctate condition of more recent origin. A group of punctæ was excised for microscopical examination and the scar had become deeply pigmented, almost black.

The microscopical appearances of sections, which were cut in series through the whole piece of tissue and stained with hæmatoxylin, were as follows: The epidermis showed no noteworthy changes. In the corium it was noticed (1) that there were several dilated blood-vessels with some slight proliferation of their endothelial walls and a few lymphocytes around them. At one point immediately below the epidermis there was a localised dense cell-infiltration. Beneath this infiltration there was one particularly noticeable blood-vessel, which extended across the section almost for the whole width of the infiltration. Here and there sweat-ducts, and at the margin of the infiltration a hair follicle, passed through the infiltration. The cell-infiltration was made up chiefly of lymphoid cells with a few epithelioid cells. There were no pigment-cells in or just below the epidermis, but at the lower part of the cell-infiltration, and in and around the walls of the blood-vessels, were numerous spindle-shaped groups of greenish-brown granules, some with a cell-nucleus at the centre of the group. These were probably pigment cells, but as the whole series of sections was stained with hæmatoxylin, no sections were examined unstained and none were stained to show mast-cells.

It did not appear that the infiltration occurred especially about the sweat-ducts (as Schamberg suggested), nor about a hair-follicle (as the clinical appearances suggested.)

In conclusion: Schamberg's disease was a slowly progressing inflammatory affection. There was a dilatation of blood-vessels, together with localised areas of cell-exudation or proliferation. The pigmentation was not due to blood-changes from purpuric hæmorrhage, but to the spindle-shaped collection of pigment-granules observed in the hæmatoxylin-stained sections. That "stasis" was not necessarily a factor in its causation was shown by the fact that it had occurred upon the forearms as well as upon the legs. The symmetrical distribution of the lesions on the arms and legs, and the histological findings, distinguished them from those of angioma serpiginosum.

BIBLIOGRAPHY.

FOX, COLCOTT.—*Brit. Journ. Derm.*, 1905, xvii, p. 416.
FREEMAN.—*Ibid.*, 1902, xiv, p. 425.
LITTLE, GRAHAM.—*Ibid.*, 1914, xxvi, p. 357.
SCHAMBERG.—*Ibid.*, 1901, xiii, p. 1.
WHITFIELD.—*Ibid.*, 1914, xxvi, p. 334.

DISCUSSION.

Dr. **BUNCH** said he had seen this case before, and then he was not sure whether the inflammatory condition was not due to the congestion caused by the varicose veins which this man suffered from, and that it was in fact a genuine case of Schamberg's disease.

Dr. A. **WHITFIELD** remarked that angioma serpiginosum was described by Sir Jonathan Hutchinson as an angioma so far as he knew, but he did not know that any histology supported his description. He thought it was identical with this disease, but he did not regard it as an angioma. He believed Schamberg's disease to be a capillary angiosclerosis with secondary inflammatory changes.

Dr. H. G. ADAMSON showed a case of *multiple rodent ulcer, possibly of sweat gland origin.* (A report of this case, with a description and drawings of the microscopical findings, will be published in a subsequent number of the Journal.)

Dr. A. WHITFIELD described cases of *Pruritic dermatitis caused by infection of mange from the kitten.* Cases of transference of diseases of animals to human beings had always a somewhat special interest, and in this short series of cases there was a rather curious coincidence in addition.

On March 10th, 1916, a gentleman developed a pruritic eruption; he consulted a well-known dermatologist, who made the diagnosis of scabies and treated him with success. On June 20th his wife's maid developed a pruritic eruption, and a few days later his wife herself became affected with a somewhat similar eruption. Shortly after this one of the children who had been staying in the country came to London and developed an eruption after her return to the country. The doctor who attended the family was puzzled by these cases as, although the method of spread suggested scabies, he was unable to recognise the eruption as that of scabies. He therefore brought the lady and her maid to him for his opinion.

When he saw these two patients their condition was as follows: The lady had a patchy eruption of small papules, about a millimetre in diameter, surrounded by an oval zone of erythema and in some instances surrounded by a minute pin's-head-sized vesicle or serous crust, the resulting lesions being not unlike those of varicella on a very small scale. These lesions were never very closely aggregated, but were in rough groups, so that the individual lesions occurred about ½ in. from each other, and then there would be a large area, about 8 in. long, of unaffected skin, and then another rough group of lesions. The distribution was on the forearms, the upper arms, the thighs, the breasts, but not the nipples, the abdomen and the scalp, but not the face. The fingers and the wrists were free. In the maid the lesions were precisely similar, but the scalp was not affected. Pruritus was intense, but was not very specially worse at night.

The appearance of the eruption immediately suggested to him mange caught from the dog, of which he had been lucky enough to see a large number of cases, and he asked if the patient had a dog. She replied in the negative, but stated that they had a kitten who scratched a good deal, He therefore sent for the kitten, and found it rather scurfy, especially behind the ears and on the face, and he removed some of the scales and put them under the microscope. He was lucky enough to find both the acarus and a run, including eggs and fæces, in one cf the earlier specimens. The kitten was chloroformed on the spot, the patients were put through a mild form of treatment for scabies, and he had since heard that there had been no recurrence of the disease.

The first point that suggested itself at once was: What was the nature of the original attack on the husband? He had no doubt that this was ordinary scabies, since the husband developed his eruption on March 10th and the kitten was not born until about May 14th—*i. e.*, about two months after the husband was affected. This seemed to him to be a rather curious coincidence, since two different acarine infections in the same family within three and a half months must be very uncommon. Moreover, if it had not happened that the animal in question was so very young, one would never have been certain that the disease in the husband was not of the same nature. Lastly, although mange caught from the dog was certainly far from rare, this was the first instance in which he had identified the infection as coming from the cat. He would say in passing, that he regarded infection with mange from the dog as common, and with ringworm as rare, while from the cat the infection with ringworm was common and with mange rare.

He only remembered seeing one outbreak of mange in cats on any large scale, and this was due to the exceptional opportunities of studying skin disease in animals that he had had for some years owing to the kindness of his friend, Prof. Hobday. In this instance the disease ran through a valuable cattery of chinchilla Persians, and either the disease, or his too enthusiastic treatment, resulted in the death of about four hundred pounds worth of cat. He found the acarus likewise in the samples of cat submitted to him on that occasion, and it was very much smaller and of not quite the same shape. On looking up this question he found that the cat suffered from two forms of acarus, one almost indistinguishable from the ordinary parasite of human itch, but now believed to be a distinct variety; a second, known as acarus minor, which usually caused the death of the host. He had no doubt that the very small, peculiar shaped acarus that he obtained in the chinchilla epidemic belonged to this variety and may have been responsible, rather than his treatment, for the high mortality.

It interested him to find the extremely superficial position of the run in this kitten; it was in no sense a burrow, but rather a pathway among the scales. Hence the name occasionally given to it of "acarus squamosus." It appears that the position of the acarus and run in Scabies norvegica, which he had not seen, was somewhat similar.

Dr. S. E. **Dore** asked if Dr. Whitfield regarded this acarus as the human acarus. Fantham, Stephens, and Theobald, in their book on *The Animal Parasites of Man* (pp. 319–521), stated that the human acarus can be artificially transmitted to horses, dogs, and monkeys, but not to cats. The sarcoptes minor, however, which inhabited cats and rabbits, caused an eruption in man lasting about a fortnight. He thought that it was more likely to be the small acarus in this case than the ordinary human acarus.

Dr. **Whitfield** (in reply) said that this was not the small acarus; he did not think it was the human acarus. He looked up the book mentioned a few weeks ago, and they said all these animal acari were alike. But the acarus minor was much smaller, and was not quite the same shape.

Dr. J. H. **Sequeira** showed a case of *resistant eczematous eruption associated with erythræmia*. The patient, W. M—; aged 28 years, a lift attendant, was transferred to his care by Dr. Leyton in February, 1916. He had previously been under Dr. Pringle for his skin-affection. Since 1912 the patient had noticed that his face was getting darker, and in 1914 his face, arms, and legs became purplsh in colour, the tint being deeper in cold weather. In 1915 Dr. Leyton's notes describe the face as being "plum-coloured." The patient was dyspnœic, the fingers were clubbed, and there was œdema of the ankles. A red macular eruption was present on the face and chest, and there were infiltrated plaques on the legs. The cardiac dullness was not increased, the heart sounds were clear, but there was tachycardia. The blood-pressure was 120 mm. The edge of the liver could be felt below the costal margin, but the spleen was not palpable. There was no ascites. The blood examination showed a persistent polycythæmia, varying from 7·5 millions to 10 millions, the average of five examinations being 9 millions. The patient complained of severe headaches, which were relieved by venesection from time to time. The urine was free from albumin.

The patient had been under his care for the greater part of the year. He had a dark red, slightly infiltrated, papular eruption with a moderate degree of scaling all over the abdomen, arms, and thighs. Below the knees, however, the eruption was different and of a deep purplish tint with some areas exuding serum, but for the most part covered with large flaky scales. The eruption everywhere itched intensely, and that on the legs caused a sensation described by the patient as "aching."

The case had proved exceedingly resistant to the usual forms of treatment, and was shown with a view to eliciting opinions as to its chronicity being dependent on the blood condition.

Dr. F. PARKES WEBER said that this was not, in his opinion, a case of erythræmia (primary splenomegalic polycythæmia). Owing to the clubbing of the fingers, the history of chronic bronchitis, and the absence of splenomegaly, he had no doubt that this was a secondary polycythæmia, due to old lung trouble. Such cases were examples of what he preferred to call "cardio-pulmonary" secondary polycythæmia.* In true erythræmia, as distinguished from erythrocytosis (secondary polycythæmia), the spleen was practically always enlarged (whence the term "splenomegalic polycythæmia"). In the present case he suspected that there was more pulmonary emphysema and pulmonary fibrosis present than was evident by ordinary examination, and the prognosis was not good. In such cases the red cell count was often as high as in (primary) erythræmia. He did not think that the skin disease was causally related to the blood condition in Dr. Sequeira's case.

Dr. J. H. SEQUEIRA showed a case of *sebaceous adenoma (Pringle type) in mother and daughter*. The younger patient, a girl, aged 13 years, was sent to the exhibitor for treatment. She was one of four children, the others being unaffected. She had the characteristic, symmetrical, bright red nævoid lesions affecting the nasolabial sulci and adjacent parts of the cheeks. She had also a red scar about an inch square in front of the left ear where treatment by carbon dioxide snow had been applied at another hospital. The child had also several pigmented moles, but there were no lipomatous swellings above the iliac crests. The child was very nervous and rather dull.

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* *Cf.* F. P. Weber, "On the Prognostic Significance of Secondary Polycythæmia in Cardio-pulmonary Cases," *Lancet*, 1913, i, p. 1307. In none of the cases was any skin eruption noted.

The mother, aged 32 years, had the cicatrices of an exactly similar affection which involved the naso-labial regions and the cheeks. The cicatrices were the result of treatment by electrolysis at a special hospital. She also had other nævi, but no swellings above the iliac crests. She did not know of any other member of her family being affected.

The **President** had seen two cases of this kind successfully treated by the repeated application of strong carbolic acid (90 per cent.) to the separate lesions.

Dr. W. **Knowsley Sibley** showed a *case for diagnosis.* G. N—, a strong, healthy man, a gamekeeper, aged 48 years, who had a good family history, had suffered from the present eruption for some nine years. The condition commenced on the outer side of the right thigh, and gradually extended to both legs as far as the ankles, and had of recent months appeared on the upper eyelids. At the present time the eruption was situated more or less symmetrically over both shoulders, arms, buttocks, legs, thighs, and upper eyelids. The chest, back, and the rest of the face were free. There were no lesions on the mucous membranes. The lesions were slightly irritable at times, but never excessively so. They consisted of small bright red papules and follicles, closely crowded together, with no tendency to coalesce, except on one small area on the right forearm, but with a very distinct curved margin of distribution, and sharp lines of demarcation from the normal skin area, especially marked over the deltoid and scapula regions. Several of the smaller follicular lesions were slightly pustular, probably the result of local applications. The glands in the axillæ and groins were enlarged.

A section of a papule taken from the left thigh revealed the following histology: The layers of the epidermis appeared to be normal, except over the region of the nodule. Here the stratum corneum was thickened and infiltrated with cells. Beneath this layer there was a cavity present; which was formed in the stratum mucosum, and which appeared to be infiltrated with cells of the mononuclear and polymorphonuclear type. In the dermis there was a dense mass of cells which here and there showed a tendency to coalesce and form small giant cells. The blood-vessels were dilated and surrounded with cells.

The PRESIDENT remarked that this was a very unusual case, and he had no recollection of seeing one at any time which exactly corresponded with it. The lichenoid character of the lesions was well marked, but it was possible that the persistent innunctions of vaseline for years had modified the original character of the disorder.

Dr. F. PARKES WEBER hoped Dr. Sibley would report the blood count, because the glandular enlargement in the axillæ and groins was suggestive of leukæmia, and some of the cell-infiltration in the skin lesion (shown under the microscope) might be lymphocytic.

Mr. McDONAGH thought it was a case of aleukæmic lymphocytoma. The skin lesions were typical of that condition, and the patient had generalised adenitis. The lymphatic glands were most enlarged and hard in the inguinal regions, where they were noticeable before the rash appeared. It was strange to find, in these cases, that the lymphatic glands which appeared to become enlarged first were those in the inguinal regions. The picture given by the histological specimen would fit in well with the diagnosis above mentioned. To prove the correctness of the diagnosis, or the reverse, it would be necessary to examine a lymphatic gland.

Dr. GEORGE PERNET showed a case of *severe iodide eruption*. The patient was a man, aged 50 years, who attended the West London Hospital on October 17th, 1916, for an eruption involving the face, hands, and feet, and of nine weeks' duration. It started with what the patient called "blisters" in the left palm, with "yellow tops," and containing matter. This was rapidly followed by similar eruptive elements about the hands, palms and backs, and then about the feet. In these situations the lesions had flattened down and dried up. Some of these were about the size of a florin. Looking at the feet alone, the lesions reminded one to some extent of a subsiding keratodermia blenorrhagica; but it might be said, in passing, there was no evidence of gonorrhœa, but the patient stated he sweated pretty freely. The face and scalp had been more recently affected, and there the lesions were characteristic of a severe iodide eruption, being raised, purulent, and crusted, and about ½ in. and less across. Smaller purulent elements were scattered about the scalp. A fortnight before the eruption started the patient had taken a bottle of Clarke's Blood Mixture (apparently 8 oz. size, which would represent 52·5 gr. of iodide of potassium according to the Martindale's "Extra-Pharmacopœa"). Urine *nil*.

Dr. S. E. Dore showed a case of *localised sweating of the face and (?) hidrocystoma.* The patient was sent to his department at Westminster Hospital by Mr. Arthur Evans. He was aged 44 years, and had suffered for two years from excessive sweating in the areas of skin supplied by the first and second divisions of the fifth nerve. The sweating was more marked on the left side and was excited by mental strain or emotion, also by hot, alcoholic, or effervescent drinks or bitters. For six months he had had an eruption of superficial grouped vesicles on the forehead just above the nose and in the malar regions, and this eruption fluctuated from time to time. He stated that it almost disappeared in the morning, but in the evening it was very noticeable. Crocker* referred to cases of hidrocystoma or dysidrosis of the face occurring in association with localised sweating of this type, but it was doubtful whether the eruption in this case could be called by that term, or whether it was a superficial sweat eruption akin to sudamina. He was apparently a strong, healthy man. He stated that he suffered from malaria twenty-three years ago in Malta, and he had also been in the habit, during recent years, of indulging frequently in Turkish baths. There was no history of injury and no other symptoms referable to the sympathetic system. He would be glad of suggestions as to treatment. He had taken belladonna for a short time without any beneficial effect.

The President suggested that a strong solution of boric acid with rectified spirit was sometimes useful in these cases, as also the application of a mild continuous electrical current.

Dr. F. Parkes Weber showed a case of *multiple idiopathic hæmorrhagic sarcoma (Kaposi)*.

(This case is described in Dr. Parkes Weber's paper on p. 312 of this number (Case 3.)

Dr. J. H. Stowers (President) showed a case of *circumscribed sclerodermia (morphœa) in a child.* The patient, aged 7 years, the elder of two children, was sent to him by Dr. W. F. Addey. She was born at full time, and nothing unusual occurred at or near the period of her birth. The parents were healthy. In October, 1915 the mother first noticed a faint white streak slightly to the right of the middle line of the forehead, extending from the base of the nose upwards to the scalp. Shortly afterwards an impetiginous affection developed, involving the nostrils. The child was extremely neurotic, and it was stated that a few weeks before the disorder was noticed she had been suddenly awakened out of her sleep and greatly terrorised by the explosion of bombs during a Zeppelin raid at midnight in the neighbourhood in which she lives.

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* *Diseases of the Skin*, 3rd edit., p. 1040.

The disease, which had greatly increased, now extended from the junction of the lower and middle thirds of the bridge of the nose upwards on the right side into the scalp, and measured 5½ in., and laterally, for about 3½ in. the forehead was involved. The skin of the upper eyelid was free. The scalp was more markedly sclerosed than the skin of the face, being harder and more tense. The characteristic pearly whiteness of the skin, with a violaceous margin, was very observable, sensation being much reduced. At this time the skin of the forehead and nose on the right side was but little less elastic and yielding than the left, which was normal. It had been stated that this affection, when involving the forehead and scalp, occurred, for some unknown reason, more frequently on the left side than the right.

Dr. S. E. Dore showed a case of *secondary malignant ulceration of the skin*. This woman, aged 42 years, was under the care of Mr. Peart, who asked him to see her. She had half her breast removed for "scirrhus" seven years ago, the operation being completed eighteen months later. The present lesion was said to have begun two years ago as a blister, and she stated that she had a similar lesion on the chin, which disappeared, leaving a healthy scar. It consisted of a flat oval plaque of firm thickened brownish-yellow tissue, with a sharply defined border, raised about $\frac{1}{8}$ in. above the surface, and measuring 2 in. in length and 1½ in. across, situated on the left side of the chest below the transverse linear scar left by the operation. In the centre was a shallow circular ulcer $\frac{3}{4}$ in. in diameter. In addition there were two small nodules, covered by brown scabs, at the lower anterior axillary border. The question arose as to whether the lesion on the chest was independent of the original tumour, or was a secondary malignant growth of the skin. In spite of its somewhat unusual appearance, there seemed to be little doubt that the latter was the explanation of the condition. So far no treatment has been adopted, and he would be glad to hear views as to whether excision, radium, or X-rays was most likely to prove beneficial.

Dr. J. M. H. MacLeod considered that involution of the skin lesion might be effected by large doses of radium. He considered the skin lesion as secondary to some deep-seated recurrence, however, and considered the removal would be only of temporary benefit.

The President agreed as to the nature of the case, and thought that Dr. MacLeod's suggestion that radium should be generously administered might be helpful; but unless he had had Dr. MacLeod's experience he would have recommended excision. The disease was of such serious nature that he doubted if any treatment would prove successful owing to the involvement of deeper structures, including deposits in the mediastinum.

CURRENT LITERATURE.

ANATOMY OF THE SKIN.

THE SMOOTH MUSCLES OF THE SKIN OF THE CHIN. S. Giovannini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1916, fasc. iii, p. 105.)

The author undertook this investigation in order to see whether he could confirm the statement made by Diesing some years ago that the skin of the chin contained no muscle fibres. He examined skin from an adult man with a beard, and found that muscle fibres are certainly present, but that they are more or less few in number. They are not only found in relation to the follicles of the large as well as the small downy hairs, but may also occur apart from hairs. Some of the muscles in relation to the follicles were rudimentary, and were not long enough to become inserted into the follicle. R. C. L.

CONGENITAL CONDITIONS.

CONTRIBUTION TO THE STUDY OF CONGENITAL CIRCUMSCRIBED HYPERTRICHOSIS OVER THE VERTEBRAL COLUMN WITHOUT SPINA BIFIDA. C. Vignolo-Lutati. (*Giorn. Ital. d. Mal.Ven. e della Pelle*, 1915, fasc. ii, p. 172.)

The author reports two cases of this rare condition. Both were in men. In one there was a hairy patch over the lower lumbar and upper sacral region, with no alteration in the skin otherwise; in the other there was a large pigmented nævus over the greater part of the back, with patches of long hair in the middle line in the mid-dorsal and lumbar regions. In both cases no alteration in the bones of the spinal column was to be made out. The author comes to the conclusion that cases of hypertrichosis, with or without appreciable spina bifida, sometimes combined with diffuse pigmentation, are the result of a circumscribed persistence of the fœtal lanugo hairs. This persistence of the hairs he ascribes to some disturbance, probably through the nervous system, of the development of the embryo. R. C. L.

NÆVUS ANÆMICUS. J. E. LANE. (*Journ. Cut. Dis.*, 1916, August, xxxiv, p. 602.)

IN this contribution a case is reported of the rare conditon first described in 1906 by Vörner as Nævus anæmicus. He recorded four cases of it, and differentiated it from Albinismus partialis. Nanta and Lavau of Audry's clinic collected seventeen published cases, and recorded one of their own in France. The case which forms the subject of this paper is the first to appear in American literature, while, so far as the reviewer is aware, no case has yet been published in Great Britain.

Lane's case was that of a woman, aged 30 years, who presented small white spots on the right cheek. These spots were six in number, and had been noticed since birth. They were best seen when the face was either flushed from heat or exertion, or had been exposed to cold, but at other times were hardly perceptible. The uppermost spot was situated below the outer angle of the eye, and the remaining five were grouped beneath it. They were all nearly circular in shape, but with somewhat irregular borders, and the largest of them measured about 1 cm. in diameter, whilst the others were about half that size. The surrounding skin was normal, except that the vessels at the border of of the largest spot were slightly telangiectatic. The skin of the spots themselves was normal, except for its colour; the hairs were present on it, and were of the same colour as on other parts of the face, and the pores were of the same size as those of the surrounding skin, and plainly visible. The sensation was normal.

The above description bears a striking similarity to that of all the reported cases. The affection would seem to be of such trifling importance that it has usually been detected by the physician during an examination for some other disease. The spots occasionally occur singly, but are usually found in groups, which tend to have a zosteriform arrangement. Vörner, who examined the skin histologically, found that the blood-vessels were smaller than in the normal skin, and that the smaller arteries had the structure of capillaries.

Various explanations of the anæmia have been given, such as: that it is due to the inability of the vessels to dilate (Vörner); that it is a sluggish reaction of the vessels to dilation in limited areas, and the opposite of Cutis marmorata, in which the vessels are dilated and sluggish to contract (Fischer); that the actual number of blood-vessels is diminished (Stein); and, lastly, that it is due to a fœtal narrowing or obliteration of some of the vessels (Sprinzel).

The condition has to be distinguished from Albinismus partialis, from which it differs in that there is no lack of pigmentation in the affected areas. It is similarly distinguished from leucoderma. J. M. H. M.

BACTERIAL INFECTIONS.

ON IMPETIGO NEPHRITIS. HERMANN EICHHORST. (*Deutsche Archiv f. Klinische Medicin*, 1916, vol. cxviii, pls. 4 and 5, p. 462.)

EICHHORST records three examples of nephritis associated with Impetigo contagiosa of Tilbury Fox. The patients were sisters, aged 14 years, 9 years, and

6 years. All had typical impetigo involving the face and scalp, and to a less extent the limbs. Two became ill with severe hæmorrhagic nephritis about a week after the onset of the impetigo. Both had œdema of the face and limbs. One died of uræmia, and in the other (the eldest child) the nephritis lasted for two months. The third child had slight nephritis. A fourth sister, aged 2½ years, who also had impetigo, did not get nephritis. The 9-year old sister, who had slight nephritis, fell ill with diphtheria of the throat fourteen days after the onset of the impetigo, and after that had been cured and the albumin had disappeared from the urine, the albuminuria recurred. This fact led Eichhorst to believe that there might be a family predisposition to renal susceptibility to toxins. Another explanation might have been that the infection had been due to unusually strongly pathogenic streptococcus. When he first recorded these cases Eichhorst was unaware of any similar instances of the association having been reported, but he afterwards discovered references to communications by Duvernay ("De la néphrite impétigineuse," *Lyon. Med.*, April, 1908, s. 844), and by von Hutenel ("Nephritis impetiginosa," *Giorn. d. pract.* 1901, No. 4).

H. G. A.

[Duvernay's paper is abstracted in the *British Journal of Dematology*, 1909, xxi, p. 371, and references are there given to further contributions by Guinon and Pater ("Complications rénales au cours de l'impetigo," *Rev. Mensuelle des Mal. de l'Enfance*, 1908), which deals fully with the subject, and to Villattes' *Thèse de Bordeaux*, 1907, and Guiart, *Thèse de Paris*, 1908.—H. G. A.]

LEPROSY.

PRELIMINARY NOTE ON THE INTRAVENOUS INJECTION OF GYNOCARDATE OF SODA IN LEPROSY, WITH FURTHER EXPERIENCE OF ITS SUBCUTANEOUS USE. Sir LEONARD ROGERS, M.D., F.R.C.P. (*Brit. Med. Journ.*, October 21st, 1916, p. 550.)

THE author's experience of the intravenous injection of gynocardate of soda has led him to substitute it almost entirely for the subcutaneous method. Further experience is required to ascertain how far it is advisable to push the doses, but he considers that even half a grain given intravenously is likely to have a greater effect than four grains slowly absorbed from a subcutaneous injection. He believes that the intravenous method is likely to prove as great an advance on the subcutaneous method as the latter has proved on the oral administration of gynocardates or chaulmoogra oil. The selective local reactions which follow intravenous injections are very striking, and no ill effect appears to follow them. An account is given of the method of preparation and administration of the solution, and also of the further results the author has obtained after a year's experience of gynocardate of soda given subcutaneously. S. E. D.

ANIMAL PARASITES.

CUTANEOUS MYIASIS IN MAN. PORTA ANTONIO. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1915, fasc. i, p. 5.)

IN this article the author gives a very comprehensive description of the different insects and their larvæ which cause lesions in the skin. The following groups are described: (1) Sarcophaginæ, (2) Callephorinæ, (3) Hypoderminæ, (4) Œstrinæ, (5) Cuterebrinæ, (6) Gastrophilinæ, (7) Muscinæ, and (8) Anthomyinæ. Under each of these groups several varieties are also given. There is a very full bibliography of references to reported cases. The article should prove very useful for reference in cases where uncommon insects or their larvæ are found in the skin.

R. C. L.

THE LOUSE PROBLEM AT THE WESTERN FRONT. A. D. PEACOCK, M.Sc., R.A.M.C. (T.F.). (*Brit. Med. Journ.*, May 27th and June 3rd, 1916, pp. 745 and 784.)

THE writer gives an exhaustive account of the morphology and habits of the body-louse, and proposes a scheme for establishing a standard of "lousiness" by which to judge the condition of individual soldiers or of a unit. In order to estimate the best methods of the prevention and destruction of lice a large number of experiments were performed with various insecticides. N.C.I. (naphthalene 96 per cent., creosote 2 per cent., iodoform 2 per cent.) was found to be the best all-round preparation tested. It acted as a complete deterrent, and the effect of one thorough application lasted about five days. Too free use of the powder, however, causes severe smarting, especially at the fork, and it is recommended that an ointment insecticide should be used in this region. Vermijelli is an effective ointment, but requires to be applied over the whole body. Crude oil ointment, consisting of soft paraffin and crude tar-oil, gave a result of 97·7 per cent. efficiency. By using N.C.I. and vermijelli together, the ointment being smeared over the seams and fork of the trousers and the powder dusted down the shirt and trousers, the general efficiency was highly increased. N.C.I. and crude ointment gave similar results. Blue mercury ointment was unsuitable and useless as a deterrent. White mercury powder had very low killing and general efficiency, and sulphur in powder or ointment was a complete failure. With regard to the treatment of underclothing experiments showed that not more than one hundred garments should be steamed at 215° F. for three-quarters of an hour, using the horse-drawn "Thresh" disinfector, and one hundred garments per chamber at 220° F. and 5-lb. pressure for half an hour with the Foden lorry "Thresh." After boiling shirts for five minutes in water the lice were killed and the eggs become white and opaque, and failed to hatch out after fourteen days' incubation on the body. Using 1½ per cent. cold cresol solution the lice were killed after thoroughly soaking infested shirts for one hour. Chloride of lime, 7 per cent. cold solution, used for twenty-four hours, is effective, but alum, 10 per cent. cold solution, used for forty-eight hours, was a total failure. When giving baths to a large number of men treatment by steam or gas disinfection takes too long, as it is usually necessary for men to pass through the baths in a quarter of an hour, and ironing with a hot iron is the most practicable scheme. The author recommends that a definite plan of campaign against the pest should be formulated, including a centre of research under a specialist, in each army, lectures and classes for the men, and the issue of leaflets of instruction to all ranks.

S. E. D.

AN INVESTIGATION OF THE BEST METHODS OF DESTROYING LICE AND OTHER BODY VERMIN. J. PARLANE KINLOCH, M.D. (*Brit. Med. Journ.*, June 3rd, 1916, p. 789.)

THE author's conclusions are as follows :

(1) As shown by Bacot and demonstrated by the writer's later experiments, lice do not survive immersion in boiling water.

(2) Several insecticidal powders have been tested, and of these N.C.I. powder is the most destructive to lice.

(3) Of the three constituents of N.C.I. powder, naphthalene and creosote have each a strong insecticidal action. The insecticidal action of iodoform is feeble.

(4) Naphthalene appears, so far as the writer's comparative tests have gone, to be the most suitable basis for use in the preparation of a powder destructive to lice. Commercial naphthalene is more actively insecticidal than pure naphthalene, and it appears that the lethal power of naphthalene for lice is dependent in great part on the presence of hydrocarbons and coal-tar derivatives other than pure naphthalene.

(5) The immediate lethal effect of creosote when mixed with naphthalene is less than that of some other insecticidal liquids, but the longer period during which creosote continues to act more than compensates for the initial disadvantage.

(6) In addition to its feeble insecticidal activity, iodoform greatly increases the adhesiveness of N.C.I. powder for cloth. The inclusion of iodoform in the powder is accordingly justified, although similar adhesiveness of the powder is obtainable at less cost by substituting the insecticidally inert but cheaper magnesium silicate for iodoform in the powder.

(7) The insecticidal power of naphthalene-creosote powders gradually diminishes when they are exposed in the open air.

(8) The moist nature of such powders precludes their being used successfully in perforated tins, and it has not been possible to dry the powders and at the same time retain the moist and volatile hydrocarbons and other coal-tar derivatives on which the insecticidal effect mainly depends.

(9) It is desirable that naphthalene-creosote powders should be supplied in sealed tins of a uniformly small size, or of sizes suitable for the immediate requirements of a convenient number of persons proposed to be treated at one time.

(10) In experiments with gases, sulphur dioxide has maintained its reputation as the most efficient gaseous insecticide, and all lice exposed to an atmosphere of the gas die within five seconds. As ordinarily used for disinfecting purposes, and as a result of lack of penetration, sulphur dioxide cannot be depended on to kill all lice in verminous clothing.

(11) For the emergency cleansing of clothing by means of petrol, immersion of the verminous clothing in petrol remains the most suitable method. To secure the insecticidal action of the vapour of petrol a regulated oven would have to be employed.

(12) The superior value of certain chlorine derivatives of ethylene and ethane as insecticides and their non-inflammable properties indicate their use in the cleansing of verminous heads. The desired result is obtained and irritant effect

on the scalp is obviated when the hair is gone over carefully with pieces of cotton-wool moistened with either trichlorethylene or tetrachlorethane. Tetrachlorethane, although less powerful than trichlorethylene, is very actively insecticidal, and is to be preferred to trichlorethylene on account of its less irritant properties.

S. E. D.

THE USE OF INSECTICIDES AGAINST LICE. A. Bacot, Entomologist to the Lister Institute of Preventive Medicine. (*Brit. Med. Journ.*, September 30th, 1916, p. 441.)

The author gives an account of a large number of experiments on the insecticidal value of various remedies, the insects being placed in conditions as nearly natural as possible, and particular care being taken that they should have the opportunity of feeding during the tests. In order to accomplish this object the lice were placed in small bags of silk gauze in wire-gauze frames, and suspended between the skin and clothing in various parts of the body. Preliminary trials with naphthalene showed that the diffusion of vapours over the body-surface beneath clothing is restricted to a very small area round the centre of distribution, in so far as it had any effect on lice. In order to test the relative effects of contact and diffusion of a number of remedies with greater accuracy, a series of five wire-gauze frames fixed to a flexible bar were used, and so arranged that the whole could be tied firmly against the body, the gauze on one side coming in contact with the skin so that the captive lice could feed, Lice were placed in all five chambers, two of the latter acting as controls. Most of the substances tested were those in common use, *e. g.*, naphthalene, sulphur, cresylic acid, iodoform, vermijelli, etc. Cytisine, an alkaloid showing similar physiological properties to those of nicotine, and extracted from the seeds of gorse and laburnum, was also tested. The net results of the trials was to suggest that the diffusive effects of all the substances, except possibly naphthalene, is so slight as to reduce them all to a common level of contact remedies. Attention was next directed to remedies of low cost and slow action with a view to testing their effectiveness in preventing the breeding of lice when used to impregnate garments. In these experiments it was necessary to keep adult lice confined for several days in order that there might be time for egg-laying and for the eggs to develop. Shallow card boxes were used instead of the wire frames, the open top of the boxes being covered with fine chiffon, through which the insects fed. The boxes were lined with flannel shirting material dipped in the solution it was desired to test, and dried off rapidly. The practical effect of impregnating cloth was found to last about six or seven days, the smell possibly acting as a deterrent for a few days longer. Although cytisine was experimentally successful, it had the insurmountable objections of a possible toxic action and of high cost of production. The trials suggested that that a practical remedy may be found for preventing the spread of lice among troops by the use of a crude liquid carbolic acid and soft soap emulsion for the impregnation of shirts and underclothing. The emulsion should consist of 45 per cent. to 50 per cent. of soft soap combined by heating with 50 per cent. to 55 per cent. of crude carbolic acid ; the strength of the solution used to impregnate the garments should be 5 per cent. of the emulsion in warm water, 3 per cent. being too weak for practical use, while solutions above 5 per cent. might irritate the skin. After dipping, the garments should be wrung and thoroughly dried before wearing. A normal-sized shirt after wringing will retain about 500 to 600 c.cm. of the solution, and the cost would probably, apart from labour, be about one halfpenny per shirt. A test on a practical scale is required to ascertain (1) what percentage of men are likely to have irritable skins which might be susceptible to the small percentage of cresols in the shirt, and (2) the efficiency of the remedy to keep men free from lice in the field. S. E. D.

TREATMENT OF SCABIES BY SULPHUR VAPOUR. Major JOHN BRUCE, R.A.M.C.(T.), and Captain STANLEY HODGSON, R.A.M.C. (*Brit. Med. Journ.*, August 5th, 1916, p. 177.)

THE writers figure and describe a cabinet which they have used for twelve months for the treatment of scabies by sulphur dioxide gas. This method they have found to be simple, swift, and efficacious. The patient is scrubbed with soft or yellow soap in a hot bath and is then transferred to the cabinet, in which he is placed with his head protruding through an aperture in the roof, the sliding board being adjusted, and a wet towel applied round the neck to prevent escape of fumes. A Jeyes's large sulphur candle is placed in the corner of the box, lighted, and the door closed. The patient is exposed to the vapour for fifty minutes, his clothes, blankets, etc., being meanwhile disinfected. No feeling of discomfort is experienced unless an antiseptic has been added to the bath, in which case irritation of the scrotum, axillæ, and other parts may be produced. A slight general desquamation often follows the treatment. Freedom from itching is immediate. The writers have treated in this way over two hundred cases, and have had about 2 per cent. returns. The great merit of the method is that cases can be sent back to their unit on the same day as they are received and resume duty the next day. As many as twenty cases have been treated in a day in one box. S. E. D.

VASCULAR AFFECTIONS.

A CONTRIBUTION TO OUR KNOWLEDGE OF PURPURA ANNULARIS TELEANGIECTODES (MAJOCCHI). MARIO COPELLI. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1915, fasc. i, p. 70.)

Two cases of this peculiar disease are reported, the one very fully, the other less so. There are good illustrations of the skin eruption and photographs of the microscopic findings in the skin. The author agrees with the previously expressed views of others that the condition is a chronic intoxication leading to a sclerosis of the cutaneous and subcutaneous arteries, producing an obliteration of the vessel lumen. Added to these signs of chronic intoxication there may be signs of a more acute intoxication, which causes swelling of the endothelium, degeneration or simple necrosis of the middle coat, and breaking up of the elastic fibres in the vessel wall. In about a third of the cases tuberculosis is said to be associated with the condition. In both the author's cases there was a definite history of tuberculosis in the families, and in each case there was a tuberculous lesion, in one in the lung and in the other in the glands. R. C. L.

THE TREATMENT OF FROST-BITE WITH ACTIVE HYPERÆMIA.

Ermino Ghirlanda. (*L'ospedale maggiore*, January, 1916, p. 12.)

The author reports very good results in cases of frost-bite amongst Italian soldiers. In cases where the ordinary methods of massage with snow, spirit, electricity, movements and baths did no good, he found that energetic treatment daily with hot air at a temperature of 90°–100° F. produced very good results. This treatment was often continued every day for a month or so. The œdema and cyanosis rapidly disappeared, incipient moist gangrene was checked, necrotic parts became quickly detached, and ulcerated areas healed.

R. C. L.

AFFECTIONS OF HAIR AND NAILS.

MONILETHRIX.

G. M. MacKee and I. Rosen. (*Journ. Cut. Dis.*, 1916, June and July, xxxiv, pp. 444 and 506.)

In this paper, which was read before the Annual Meeting of the American Dermatological Association at Washington in May, 1916, a comprehensive description of this somewhat rare affection of the hair is given, based on a review of the literature. Six new cases are reported, and the paper is well illustrated with photographs of both the clinical and microscopical appearances. The reported cases are analysed, and there is a full bibliography. J. M. H. M.

DYSTROPHY OF THE NAILS IN MALARIA (TRANSVERSE SULCI).

Bosellini. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1915, fasc. iii, p. 255.)

The author reports a case where all the nails of the hands showed a deep sulcus towards their upper ends. Two months previously patient had suffered from an attack of malaria, which was treated with quinine. Although several conditions are known to produce transverse depressions on the nails, this is the first case where it followed an attack of malaria. The author attributes the change to a suspension or alteration of the nutritive or proliferative function of the malpighian layer, more particularly in the nail-forming zone. This change in the nail supports the physiological facts known about the growth of the nails, that the nail itself is formed from the whole surface of the malpighian layer on which the nail rests, but the most active production of nail substance takes place at the base underneath the nail fold. R. C. L.

FUNGUS INFECTIONS.

PSEUDO-ACTINOMYCOTIC FORMATIONS PRODUCED EXPERIMENTALLY WITH ACHORION SCHÖNLEINII AND TRICHOPHYTON VIOLACEUM.

F. Radaeli. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1915, fasc. v, p. 413.)

In this research the author confirms work previously done by others. A pure culture of *Achorion schönleinii* from a case of favus, when inoculated into the vein of a rabbit, causes nodules in the lung. These nodules are granulomata with necrosis. In the centre of these there form masses of fungus with radiating filaments, resembling what is seen in actinomycosis. Similar lesions were found to be produced in the lung by intravenous injection of *Trichophyton violaceum.*

R. C. L.

RINGWORM IN THE PROVINCE OF NAPLES. Alessandro Chieffi. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1916, fasc. iii, 140.)

Chieffi gives a very thorough account of the different forms of ringworm met with in the Province of Naples from 1906 to 1915. He divides the cases into Trichophyton, Microsporon, and Favus cases. In the nine years under revision he saw 580 cases due to the Trichophytons. Tinea barbæ formed the largest group of these cases (47·75 per cent.). Next in frequency came large spored Tinea capitis (27·06 per cent.), and of these cases 11·4 per cent. were Kerion cases. The remaining 23·96 per cent. were cases of Tinea corporis, of which the erythemato-squamous type was the most common. Ringworm of the finger-nails was seen in seven cases out of 580. In all cases cultures were made to ascertain the kind of Trichophyton present. The Tinea barbæ cases were found to be due to *Trs. rosaceum, acuminatum, violaceum,* and *gypseum asteroides*; the Tinea capitis cases to *Trs. acuminatum, violaceum, craterifrome,* and *gypseum asteroides*; the Tinea corporis cases to *Trs. rosaccum, violaceum, acuminatum, gypseum asteroides,* and *umbilicatum.* Of these different Trichophytons the *Trs. rosaceum, violaceum,* and *gypseum asteroides* were much the most frequent. The author found that in the large-spored ringworms a specific clinical lesion could not be attributed to any one form of the fungus. The *Tr. gypseum asteroides*, for example, is the commonest fungus in Naples, whereas it only occurs rarely in other regions. It was isolated from several clinical forms of the disease in different parts of the body. It occurred sometimes in markedly inflamed lesions, at other times in the torpid type of eruption. It was obtained from such different clinical lesions as kerion of the scalp, dry scaly ringworm of scalp, Tinea barbæ (both the lumpy and the erythematous forms), and Tinea corporis of the dry, scaly, and vesico-pustular types. The author also does not agree with Sabouraud that the suppurative types of ringworm are associated with animal infections, as he has often found it to be otherwise.

In contradistinction to the numerous large-spore ringworms observed by Chieffi, he only met with one case of Microsporon ringworm. This was in a case of ringworm of the scalp, and was due to the *Microsporon lanosum.*

Favus, however, was met with relatively frequently. During the nine years 281 cases were observed. It occurred most frequently as Favus of the scalp. In most cases the whole scalp was affected. In 1·1 per cent. of the cases the lesion occurred on the body and in 0·28 per cent. in the nails. From all these cases only one type of fungus was isolated, viz., *Achorion schönleinii.*

For further details of this very thorough investigation I would refer those interested to the article itself.

R. C. L.

NOTES ON A NEW ULCERATIVE DERMATO-MYCOSIS. Major Aldo Castellani, M.D., M.R.C.P. WITH REPORT ON THE CAUSATIVE FUNGUS. Prof. E. Pinoy, Pasteur Institute, Paris (*Lancet*, October 7th, 1916, p. 486.)

The author describes a peculiar ulcerative condition which he has met with in Ceylon since the year 1907. In a well-marked case ulcers are seen practically all over the body, but on the face, scalp, palms, and soles they are in small numbers, or altogether absent. The ulcers are generally sharply defined, roundish or oval, with red, granulating fundus. In certain cases there may be abundant purulent secretion, and the ulcers are often covered by thick yellow crusts. Gummata-like nodules and furuncle-like lesions may also be observed. Some of the superficial lymphatic glands are often enlarged. The lesions are not as a rule, very painful, and there is little or no itching. The general condition of the patient is not seriously affected for a long time, but he often complains of weakness, and general discomfort, and is unfit to attend to his work. In two cases in which the blood was investigated red blood corpuscles and hæmoglobin were slightly below the normal, and in one case there was eosinophilia (5 per cent.). This feature of the blood may, however, have been due to intestinal parasites, the stools containing eggs of ascaris. The urine did not contain either albumin or sugar. The course of the disease is long, and if left untreated there is apparently not much tendency to spontaneous cure. Most of the patients came with the diagnosis of syphilis, but in none of them except one was there a history pointing to that infection, and in two of the cases in which a Wassermann test was carried out the result was negative. Moreover, scrapings from the ulcers never showed spirochætes, and salvarsan and mercury have no beneficial effect on the condition.

The fungus was investigated by Prof. Pinoy, who proposed to include it in the genus Accladium, and call it *Accladium castellanii*. The growth consists of small roundish masses covered by spiculated formations consisting of erect straight filaments, parallel or interlacing. These filaments are approximately 2 microns in diameter and carry laterally pseudoconidia of variable shape, cylindriform, pyriform, or spherical, and attenuated in size at their points of insertion. Most of these pseudoconidia are 4 microns long with a breadth of 3 microns. This type of fructification recalls the type *Accladium* described by Bodin in some species of the genus *Trichophyton*. The pseudoconidia become detached and then develop by sprouting, and mycelial filaments are formed. Certain filaments produce spherical chlamydospores arranged in small strings as found in certain fungi of the genus *Fusarium*.

As regards the treatment of the condition, potassium iodide acts fairly well. It should be given in full doses, gr. xx three or four times daily, and acts better if the patient is given a salt-free diet as first suggested by Prof. Pinoy in other dermato-mycoses. Siodin and other similar preparations may be tried if potassium iodide is not well borne, but are not so satisfactory. Locally, it is sufficient to keep the ulcers clean by dressing them with weak mercury perchloride lotion. Ointments are badly borne in most cases.

S. E. D.

TROPICAL GRANULOMATA.

A CASE OF ULCERATING GRANULOMA SUCCESSFULLY TREATED BY INJECTIONS OF ANTIMONY. George C. Low, M.D., and H. B. Newham, M.D. (*Brit. Med. Journ.*, September 16th, 1916, p. 387.)

The authors discuss the history of the use of antimony intravenously in the treatment of various tropical diseases, and point out that Aragao and Vianna were the first to employ this drug in ulcerating granuloma in 1913. Notes are given of a case treated successfully by them in this manner. The patient was a man aged 36 years, who had a deep crateriform ulcer on the glans penis contracted from a black woman on the Gold Coast. Injections of antimonium tartaratum, varying from 1 to 2½ grs., dissolved in 2 oz. of normal saline, were given bi-weekly, and were well borne. It was necessary to give 53½ grs. in order to effect a complete cure. X-rays were not employed, as the authors wished to try the effect of the antimony alone.

The case had been diagnosed as rodent ulcer and epithelioma, but the writers' experience of the condition in British Guiana enabled them to make the correct diagnosis. The patient had been treated with anti-syphilitic remedies without effect, and his reaction to Wassermann's test was negative. S. E. D.

THE TREATMENT OF CERTAIN DISEASES OF PROTOZOAL ORIGIN BY TARTAR EMETIC, ALONE AND IN COMBINATION. Major Aldo Castellani, M.D., M.R.C.P. (*Brit. Med. Journ.*, October 21st, 1916, p. 552.)

The writer gives several modified and improved formulæ for the oral, intravenous, and intramuscular administration of tartar emetic in various tropical diseases. Its powerful action in trypanosomiasis has been well proved, and in espundia, granuloma inguinale, kala-azar, and Oriental sore it can be considered a specific. It is efficacious in yaws, especially if combined with other drugs, and seems to have a beneficial action in relapsing fever. S. E. D.

KERATOSES.

A CONTRIBUTION TO THE HISTOLOGY OF THE SO-CALLED "POROKERATOSIS MIBELLI." S. Matsumoto. (*Japan. Zeitsch. für Derm. u. Urol.*, 1916, vol. xvi, p. 293.)

The case occurred in a healthy man, aged 47 years. On the right half of the forehead and fronto-temporal region was a typical plaque of porokeratosis the size of the palm of the hand, accompanied by scarlike atrophy in some places, especially in the centre. On the part involving the hairy scalp whitish scales, like those of psoriasis, were present. The characteristic "wall" of this disease was especially marked on the forehead. There was severe itching. The duration of the disease was twenty years.

On the patch on the right side of the forehead were numerous miliary, punctiform, comedo-like or dimpled, horny papules, which were scattered and especially well developed at the periphery. Between these numerous, scarcely visible, somewhat rough, punctiform structures were observed. Four pieces of tissue were excised, imbedded in paraffin, and cut in serial section. It was found that a hyperkeratosis developed first in the follicles and subsequently in the sweat-pores. In this case therefore the follicle played as important a *rôle* as the orifices of the sweat-glands. The foregoing is an unusually good example of the fact that the follicle and sweat-gland orifices are equally affected in this disease.

A. M. H. G.

A PECULIAR FORM OF POROKERATOSIS. Shin-Ichi Matsumoto, M.D. (*Journ. Cut. Dis.*, 1916, xxxiv, p. 489.)

The patient, a man aged 26 years, presented on the palmar surface and margins of the ring finger of the left hand a number of minute horny conical elevations and depressions showing comedo-like horny plugs which were adherent, and, when forcibly detached, left a depression. Similar lesions were present on the palmar aspects of the middle and little finger. The affected skin was of a faintly yellowish colour, presenting uneven surfaces occasionally somewhat sieve-like in appearance. The condition appeared at 21, and had been progressive since.

Histological examination of the lesions showed the presence of hyperkeratosis over the opening of the sweat duct, with the formation of horny plugs consisting of closely laminated horn-cells. The epidermis in the neighbourhood of the plug was hypertrophied and the papillæ elongated. The sweat duct was not dilated in the region of the plugs.

Serial sections were cut, which showed definitely that the hyperkeratosis was located exclusively at the orifices of the sweat-glands.

The condition differed from the porokeratosis of Mibelli in that there was no tendency to the eccentric growth which characterised that condition.

J. M. H. M.

TREATMENT.

AUTOSERUM THERAPY IN PSORIASIS AND OTHER RESISTANT DERMATOSES. W. S. Gottheil, M.D. (*Progressive Medicine*, vol. xix, Nos. 3, p. 107.)

Dr. Gottheil describes his further experience in the use of autoserum therapy, which he has applied almost entirely in his private practice, as he finds it too troublesome and lengthy for dispensary work. He has treated sixty-two private patients suffering from psoriasis, eczema, pemphigus, acne, furunculosis, chronic urticaria, folliculitis, leprosy, parapsoriasis, sclerodermia, lichen planus, dysidrosis, and ulcerative radiodermatitis. The method has been used only in severe and recalcitrant cases. Autoserum therapy is, as a rule, not a curative measure, and appropriate local treatment is also required. The author reports the most satisfactory results in psoriasis, of which he has treated thirty-one cases. In this disease up to 200 c.c. of blood is removed from a vein, through a large platinum needle. This is allowed to clot, which takes from fifteen to twenty-five minutes. The blood is then centrifuged for thirty minutes at the high speed of five thousand revolutions per minute. The serum is then decanted and recentrifuged for ten minutes, and is immediately reinjected into the patient. The whole operation takes a little over an hour. Dr. Gottheil warns his readers that there should be no unnecessary delay, and states that keeping the serum in the ice chest is dangerous. The injections are given every three days or so, and the treatment is continued for three weeks. The local treatment is then undertaken. It consists in a prolonged hot-water bath and scrubbing with green soft soap once a day. A chrysarobin ointment 1 to 3 per cent. with 1 per cent. salicylic acid in vaselin is rubbed in twice a day. As soon as a reaction is produced a soothing ointment or dusting powder is applied. Dr. Gottheil states that he has never failed to clear the skin in from two to seven days.

The treatment is said to markedly postpone relapses and lessen their severity.

In chronic urticaria and senile pruritus the results of autoserum therapy are varied. In some they are described as remarkable. In a single case of ulcerative radiodermatitis the serum injections appeared to be very beneficial.

In the other conditions tried—sclerodermia, lichen planus, lepra, and pemphigus there was no benefit. J. H. S.

RADIUM EFFICIENCY IN NON-MALIGNANT SURGICAL CONDITIONS. Robert Abbe, M.D. (*New York Med. Record*, July 8th, 1916.)

The writer reviews a number of non-malignant lesions which he has successfully treated with radium.

(1) Spring catarrh of the eyelids. For this he gives fifteen minutes, once monthly, using suitable technique for the protection of the cornea.

(2) Lymphoid tumours of any description.

(3) Vocal cord papillomata and warts of all kinds.

(4) Leukoplakia of the tongue and buccal mucous membrane. In these the production of a transient painful irritation is necessary for success.

(5) The chronic abraded ulcer of the lip as well as hypertrophic conditions of the lip.

(6) Naevi. An illustration of the cure by irritative action.

(7) Keloids. He illustrates a severe case of face keloids upon which the effect of radium was admirable.

(8) Lupus erythematosus D. C.

ROENTGEN DEEP THERAPY IN MALIGNANT TUMOURS. Arthur Fenwick Holding, M.D. (*Amer. Journ. of Roentgenology*, April. 1916.)

Cases treated at the General Memorial Hospital, New York, over a period of three years are tabulated as to results.

Non-malignant diseases of the skin are mentioned, but the cases quoted are too few to need comment.

Although the article deals more particularly with carcinoma and sarcoma of various organs, the author's methods in dealing with rodent ulcer and epithelioma are interesting.

He is able to report, out of thirty-seven cases of rodent ulcer, a clinical cure in every instance. He apparently uses a Coolidge tube, and gives large doses of about 30 × screened by 3 mm. of aluminium, the equivalent spark gap being about 10 in. A case of eighteen years' duration, consisting of a large undermined ulcer situated in front of the left ear, was cured after four such treatments.

In some instances, to reinforce the radiation, he makes a preliminary use of heat. Exactly how this is employed is not clear from the description. The temperature used is 50°–55° C., and application is made for twenty minutes. An interesting example of its value is quoted.

The case was one of metastatic carcinomata of the abdominal wall. Four areas were taken :

Area No. 1 received 32 × filtered through 3 mm. of aluminium. Microscopic examination two weeks later showed "alveolar carcinoma large celled."

Area No. 2 received 50° C. of heat for twenty minutes followed by the same dose of X-rays. Microscopic examination two weeks later showed "carcinoma somewhat degenerating but active."

Area No. 3 received 55° C. of heat for twenty minutes and the same dose of X-rays. The report, after two weeks, stated "granulation tissue in ulcer ; no carcinoma."

Area No. 4 was kept as a control, and showed active carcinoma after two weeks.

As an example of the value of large doses in epithelioma one case is illustrated. This was epithelioma of the scalp (verified microscopically) of one year's duration. 100 × filtered through 3 mm. aluminium were given with a second dose of 30 ×. The result was a total disappearance of the tumour, which from the photograph appears to be the size of a tangerine orange.

The article would be of greater value if the technique were more fully explained. D. C.

SYPHILIS.

PRIMARY SYPHILIS ON THE GUMS. Prof. Achille Breda.

(*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1916, fasc. i, p. 8.)

Breda records three cases where primary sores occurred on the gums. As that situation is rarer than on the lips and tongue, he gives a full report of the differential diagnosis. The sore was situated on the anterior aspect of the gums, painless, of rapid growth, and accompanied by the usual glandular enlargement and subsequent rash. The object in reporting the cases is to draw attention to the differential diagnosis. It has to be distinguished from a swelling due to periostitis of the bone from injury, erectile tumours, cystic growths, osteoma, enchondroma, carcinoma, sarcoma, and fibroma. The accompanying enlargement of glands also leads to confusion with new growths. The syphilitic lesion can be diagnosed by its history of short duration, and the fact that it is localised to the mucous membrane. It occurs more on the anterior than the posterior surface of the gum and more usually on the gum opposite the front teeth. It is not usually large, is sharply defined, and of semilunar outline. Elevated, pedunculated, lobulated, or massive swellings are not likely to be syphilitic.

R. C. L.

THE PRINCIPLES OF THE TREATMENT OF SYPHILIS. S. POLLITZER. (*Journ. Cut. Dis.*, 1916, xxxiv, September, p. 633.)

IN this contribution the underlying principles of the treatment of syphilis are briefly described, and the methods which the writer has found most useful in his practice are thus summarised:

Specific treatment should be instituted at the earliest possible moment after a positive diagnosis has been made. Three doses of salvarsan are given, the dose being proportionate to the weight of the patient, and varying from 0·4 to 0·8 of a grm. The injections are given at intervals of twenty-fours, and followed by a course of eight weekly injections of salicylate of mercury suspended in olive oil. If the treatment be commenced before the appearance of the roseola there is a strong presumption of cure, and the case might remain under observation without further treatment. When the treatment is begun after the appearance of a rash the first course of salvarsan and mercury should be repeated after a pause of two months, and again after another similar interval. After three courses within the first year, if the Wassermann reaction remained negative, further treatment might await the reappearance of a positive Wassermann reaction. In cases which come under treatment a year or more after infection treatment should be continued until the Wassermann reaction becomes negative, and thereafter two more courses of treatment should be administered, even though the Wassermann reaction remain negative. After a year or more of constantly negative reaction without treatment the cure should be tested by a provocative injection of salvarsan and by an examination of the spinal fluid.

J. M. H. M.

A NEW REMEDY FOR SYPHILIS, LUARGOL OR "102." N. S. BONARD, M.D. (*Lancet*, September 23rd, 1916, p. 554.)

Two years ago Dr. Danysz, of the Pasteur Institute in Paris, introduced a new compound as a substitute for salvarsan in which he added silver salts and antimony to arsenobenzol. His experience shows that the drug is more active than any other arsenical compound in trypanosomiasis, seventy-five times more active than atoxyl, thirty times more active than arsenophenylglycine, and ten times more active than arsenobenzol in sleeping sickness. In syphilis, treponemata in the chancre of rabbits disappear in twenty-four hours with doses of 0·002 to 0·003 grm. of luargol per kilogramme, and the same result is obtained in men after a single injection of 0·10 or 0·15 grm. The effective therapeutic dose of luargol is thus much smaller than other arsenical compounds, and the drug can therefore be used in cases in which arsenobenzol is not tolerated. The injections are given intravenously in the same manner as salvarsan or no salvarsan. They are repeated every second or third day, beginning with 0·10 or 0·15 grm. and increased up to 0·30 or 0·35 grm., the total dose of 1·0 to 1·20 or even 1·50 grm. being given in six or seven injections. The reaction and immediate therapeutic effects of luargol are about the same as those obtained with arsenobenzol in doses three times as strong. Luargol is a light yellow-orange powder soluble in sodium hydrate, 1 grm. of the powder dissolved in 15 cm. of a 4 per cent. solution of sodium hydrate giving a dark brown, thick solution. Injections can be made in concentrated or in dilute solution, the solution being filtered in both cases.

The doses for a normal adult male are: 0·15, 0·20, 0·25, 0·30, 0·30, 0·30 grm., or a total of 1·50 grm. in six injections, repeated every second, third, or fourth day. The precautions to be taken and the contra-indications are the same as for other arsenical compounds.

The author treated 100 cases with luargol at the Lock Hospital, and all the cases did well, the therapeutic results being more rapid than with salvarsan, neosalvarsan, galyl, novarsenobenzol, or neokharsivan in every case. Out-patients left the hospital directly after the injections, and in-patients were not kept in bed. Notes of several cases are given. It is of the greatest importance that injections should not be made until the operator is assured that his needle is in the vein. If in spite of this precaution there is thrombosis, the fact is due to an excess of soda in the alkaline solution, but thrombosis may occur with any other drug if the solution is not isotonic. With regard to the so-called "nitritoid crises" occurring after intravenous injections of the arsenobenzol series, the author made experiments which showed that all monosodic or disodic products of the arsenobenzol group become turbid and yield a precipitate in the presence of chloride of sodium, carbonates, phosphates, sulphates, and chlorides of alkalies and magnesia, and more especially of phosphates. Some of these precipitates may re-dissolve in the same liquid; others remain insoluble even in an excess of soda. If a rabbit is injected with a solution which becomes turbid in a physiological solution of pure sea salt in less than ten minutes a nitritoid crisis is always produced in the animal. Fleig has shown that precipitates of arsenobenzol were present in the capillaries of the lungs of rabbits which had died from an acute nitritoid crisis; Danysz asserts that all the troubles which appear immediately or some hours after the injection are caused by the formation of a precipitate in the circulatory system, and the writer claims that his experiments with luargol also prove that in an active or passive anaphylactic crisis it is the precipitate which is the principal agent in the pathological manifestations.

Among his conclusions the author states that the formation of precipitates may be retarded and the gravity of the nitritoid and anaphylactic crises diminished (*a*) by prolonging the duration of the injections and making them in the form of highly diluted solutions; (*b*) by making the dilution with distilled water or isotonic solutions of sugar, which delay the formation of precipitates in most cases; and (*c*) by injecting at the same time anæsthetics or vaso-constrictors. As regards the products of the arsenobenzol group, the formation of a harmless or not very injurious precipitate, which manifests itself by slight troubles in from one to six hours after the injection, is an essential pre-requisite of their therapeutic efficacy. The sodic products are more active that the neutral (novo) products, and when they are well prepared and injected with the necessary precautions they are less dangerous than the neutral products. It is too soon to say that "102" is the best remedy for syphilis, as we do not know if salvarsan really cures the disease, though its great results in many cases are undisputed. But luargol is certainly a step forward in the therapy of syphilis, for it has proved its efficacy, since quite small, non-toxic, and generally harmless doses give satisfactory clinical results.

S. E. D.

ON THE PRESENCE OF DIFFERENT ANTIBODIES IN THE SERUM OF SYPHILITCS.

F. Porcelli-Titone. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, 1915, fasc. ii, p. 121.)

Investigations were made, using extract of syphilitic liver and guinea-pig's heart as antigens. Researches showed that in syphilitic sera there exist, using these two different antigens, two different elements (or combinations of elements) which function as antibodies. The Wassermann reactions which result with different antigens cannot be considered as equivalent. The author concludes that there probably exists, in addition to the antibody to the spirochæte, other antibodies produced in the tissues by reason of the infection. R. C. L

THE LUETIN REACTION IN SYPHILIS.

William Fletcher, M.D. (*Lancet*, October 21st, 1916, p. 710.)

The patients among whom the writer's investigations were carried out were all Asiatics (chiefly Chinese) of the coolie class and inmates of the Federated Malay States Government Hospitals. He found that the results of the luetin test in the group of syphilitics examined were not so frequently positive as in the cases examined by Noguchi and other observers in America. This divergence of results he attributes to (1) the deterioration from storage of the sample of luetin employed; (2) differences in the methods of treatment in force in the Federated Malay States and the United States respectively. No positive reactions were obtained in persons free from syphilis; they occurred in syphilitics only. The luetin test is so easily carried out that it would be of the greatest use in general practice if one could always decide, from the result of its application, whether a patient was or was not free from syphilis. Unfortunately this is not the case, for while a positive reaction is of great significance, a negative result does not exclude syphilis. When performed in conjunction with the Wassermann reaction the luetin test is of great value; in the early stages of syphilis the Wassermann reaction, and in the later stages the luetin reaction, is more constantantly positive. In the great majority of instances one or other reaction is positive; but in a given case, even though both reactions be negative, syphilis is not absolutely excluded. S. E. D.

THE PRESENT CONCEPTION OF CONGENITAL SYPHILIS AND ITS MODERN DIAGNOSIS.

Adolph Rostenberg, M.D. *Medical Record*, July 1st, 1916, p. 14.)

The discoveries of the last decade have necessitated a revision of our conception of congenital syphilis. Up to ten years ago germinative transmission—that is a transmission through spermatozoon or ovum or both—was generally believed to be the common mode of infection from parent to child. This was supported by Colles' law, whereby a syphilitic child could be the offspring of an apparently healthy mother, even transmitting to the mother an immunity against a syphilitic infection in later life.

Matzenauer, in his monograph in 1903, guided solely by clinical and pathological observations, doubted the correctness of this theory, and maintained that it was the mother alone, carrying the infective agent in her placenta, who transmitted the disease to her offspring. With the discovery of the Wassermann test and the finding of the spirochæte Matzenauer's placental theory was shown to be correct, as in every specific case spirochætes were found by all investigator in the intervillous spaces and the maternal portion of the placenta; moreover, the Wassermann reaction was found to be strongly positive in almost 100 per cent. of all these cases, even when the mother did not show any clinical specific manifestations. On theoretical grounds it is improbable that the spermatozoon or ovum could develop when it is invaded by living parasites, and the fact that syphilitic children with lesions on the mouth and lips could be nursed by their mothers without infecting them, whereas the same children would invariably infect a wet-nurse, is now explained by the knowledge that the mother was infected before the child was born, the apparent immunity being due to a latent infection. In view of these facts it seems justifiable to assume that there is no congenital syphilis without maternal syphilis. This being so, infection must take place through the placenta, the spirochætes being carried thence to all the fœtal organs, establishing a condition which corresponds to the early secondary stage of acquired syphilis, and setting up a severe septicæmia through their toxins to which, in the majority of cases, the fœtus succumbs before reaching its full development. Assuming that both parents are suffering from syphilis at the time of conception, the fœtus will hardly ever escape; a severe spirochætal septicæmia will cause an abortion or an early miscarriage, the macerated fœtus showing all the stigmata of congenital syphilis. If the mother alone was syphilitic at the time of conception, the offspring will be in the same danger as before, especially if the mother had no treatment or insufficient treatment and married during the first two years after infection. If the mother was free from syphilis at the time she conceived, but contracted the disease during pregnancy, the fate of the child will depend upon the period of gestation at which the infection took place.

Contradictory opinions are held in this case, some observers believing that the infection is transmitted only during the early period of gestation, others that the infection is more intense during the second period and increases as the pregnancy approaches full term. Profeta's law has also been proved untenable in the light of recent investigations. The apparently healthy children, born of mothers infected after conception, giving, according to most observers, a positive Wassermann reaction.

According to Matzenauer's placental theory the paternal infection is of no consequence unless the mother becomes infected also, but this statement has been shaken recently by the experiments of Finger and Landsteiner, who have succeeded in inoculating monkeys with the spermatic fluid of a syphilitic man, thus proving the contagiousness of syphilitic sperma in spite of the absence of spirochætes in the spermatozoon. Bab has also found a positive Wassermann reaction in the sperma obtained from syphilitics.

These findings may explain the rare cases called by Fournier infection through *choc en retour*, in which a healthy mother conceives from a syphilitic father who does not show any infectious lesions anywhere on his body, but herself, without having had a primary sore, develops early secondary symptoms in the first half of her gestation, generally followed by an abortion, the fœtus showing all the signs of congenital syphilis.

A maternal syphilis will persist in its infectivity much longer than a paternal one, and cases are seen in which a syphilitic woman, married for a second time to a perfectly man, bears him syphilitic children, such transmissions having been observed as late as twenty years after the mother was infected.

The writer gives an excellent account of the characteristic diagnostic features in a still-born and in the living syphilitic child, and concludes by making an appeal to the family physician to devote special attention to the recognition of congenital syphilis, and to demand a Wassermann test of the mother if it is suspected, since in this way only can the appalling waste of human life, due to congenital syphilis, be reduced. S. E. D.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

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INDEX OF CONTENTS.

Achorion schönleinii, pseudo-actinomycotic formations produced experimentally with (abstr.), 361
Acne, severe case of (Sequeira), 254
— vulgaris, complement fixation in (abstr.), 154
Actinomycosis (Sibley), 51
Anaphylaxis in eczema (abstr.), 152
Anthrax, a fatal case of; infection by a shaving brush (abstr.), 73
— an outbreak of, conveyed by infected shaving brushes (abstr.), 73
Antimonium tartaratum (tartar emetic), case of Oriental sore treated by, locally (abstr.), 75
Antimony, ulcerating granuloma successfully treated by injections of (abstr.), 149
Asphyxia reticularis (Unna) (Corbett), 251
Auto-serum therapy in psoriasis and other resistant dermatoses (abstr.), 354

Blood, sugar-content of, in various diseases of the skin (abstr.), 153
— the fixation of salvarsan and neosalvarsan by the (abstr.), 157

Cancer *en cuirasse*, apparently resulting from X-ray burn in treatment of an indolent breasts cirrhus (Little), 129
Carcinoma of the face, extensive, occurring in the course of a Xerodermia pigmentosa; treated by a massive dose of radium (Pringle), 253
Carcinomatous infiltration of the skin of arm (cancer *en cuirasse*), apparently resulting from an X-ray burn in treatment of an indolent breast scirrhus (Little), 129
Chemotherapy, the rationale and practice of (McDonagh), 173, 207
Chemotherapy, discussion on (Bayliss) 204, (Browning) 204, (Teale) 205, (Ward) 206, (Pringle) 213, (Harrison) 216, (Sequeira) 219, (Shillitoe) 221, (Adamson) 222, (Mills) 223, (Browning) 227, (Morris) 227 (Ward) 227, (Stowers) 228
Comedones, multiple, of frontal region in a boy (Pernet), 136
Complement fixation in Acne vulgaris (abstr.), 154

Darier's disease (Little), 263
Dermatitis cupoliformis (abstr.), 149
— herpetiformis (Dore), 133
— — (Eddowes), 268
— — in a boy (Pernet), 325
Dermatological Literature, Quarterly Survey of, 84, 163, 278, 363
Dermatolysis and Molluscum fibrosum with congenital morbus cordis and kyphosis (Sequeira), 69, 147
Dermato-mycosis, notes on a new ulcerative (abstr.), 362
Diagnosis, cases for (Sibley) 42, (Little) 63, (Dore) 66, (Sibley) 131, (MacLeod) 136, (Corbett) 250, (Sibley) 341
— microscopical specimen for (Eddowes), 53
Diphtheritic whitlow (Rolleston), 110

Eczema, anaphylaxis in (abstr.), 152
Eczematous eruption associated with erythræmia (Sequeira), 339
Emulsoid-gelation, or the "Gel" test; a new test for syphilis (McDonagh), 114, 259
Erythema serpens of piscine origin, note on a case of (Pernet), 317
Erythematous and urticarial eruptions resulting from sensitisation to certain foods (abstr.), 153

Érythème annulaire centrifuge (Érythème papulo-circiné migrateur et chronique) et de quelques éruptions analogues (abstr.), 273
Erythræmia, resistant eczematous eruption associated with (Sequeira), 339

Foods, eruptions resulting from sensitisation to certain (abstr.), 153
Fournier's secondary syphilitic analgesia, a case of (Rasch), 119
Fox, Thomas Colcott: Obituary, 93
Frost-bite, treatment of with active hyperæmia (abstr.), 352
Fungus, cutaneous lesion caused by a new (abstr.), 76

Galyl, a case of death following an intravenous injection of (abstr.), 82
— an experience of at Royal Naval Hospital, Chatham (abstr.), 276
"Gel" test, emulsoid-gelation or: a new test for syphilis (McDonagh), 114, 259
Granuloma annulare with widespread follicular eruption (Little), 40
— of the pudenda, ulcerating, the treatment of (abstr.), 75
— — ulcerative; successful treatment by tartar emetic (abstr.), 149
Graves's disease, and later myxœdema, sclerodermia associated with (Little), 124
— — sclerodermia with (Sequeira), 69
Gynocardate of soda, intravenous injection of, in leprosy (abstr.), 347
Gynocardates orally and subcutaneously in leprosy, preliminary note on the use of (abstr.), 73

Herpes recurrens of the right cheek in a boy (Adamson), 134
— zoster, followed by oculomotor paresis, mydriasis, and frontal anæsthesia (Weber), 13
— — two cases of, associated with a generalised eruption of varicella-like spots (Weber), 13
— — recurrent, of face with hemiatrophy (Trotter and Gray), 46
Hidrocystoma (?) and localised sweating of the face (Dore), 343
Hypersensitiveness, specific, or allergy in relation to certain eruptions of microbic origin (Adamson), 27
Hypertrichosis of the vertebral column, congenital circumscribed, without spina bifida (abstr.), 345

Idiopathic hæmorrhagic sarcoma (Kaposi), two cases of (abstr.), 276
— multiple hæmorrhagic sarcoma (Kaposi), three cases of so-called (Weber), 309
— — pigment sarcoma of Kaposi, case of so-called (Weber), 64
Impetigo nephritis (abstr.), 346
Internal secretions to cutaneous disease, the relation of (abstr.), 78
Intramine: A new antisyphilitic remedy (abstr.), 163
— case of tertiary syphilis treated by (Pernet), 245
— (di-ortho-amino-thio-benzene), syphilis treated by (McDonagh and Spence), 53
Iodide eruption, case of severe (Pernet), 342

Jamieson, William Allan: Obituary, 101

Keratodermia blenorrhagica (Little and Hayne), 255
Kerion Celsi, secondary Lichenoid trichophytides in association with (Rasch), 9
Kharsivan, the therapeutic and reaction effects of (abstr.), 160

Leprosy, intravenous injection of gynocardate of soda in (abstr.), 347
— preliminary note on the use of gynocardates orally and subcutaneously administered (abstr.), 73
— recent developments in the treatment of (abstr.), 74
Lice and other body vermin, investigation of the best methods of destroying (abstr.), 349
— the louse problem at the Western front (abstr.), 348
Lichen obtusus corneus (Sibley), 329
— planus? (Little), 41
— — hypertrophicus (Samuel), 266

Lichen scrofulosorum (Little), 242
— spinulosus trichophyticus (Rasch), 9
Lichenoid trichophytides, secondary, in association with Kerion Celsi (Rasch), 9
Livedo reticularis (Adamson), 281
Luargol, or 102: a new remedy for syphilis (abstr.), 357
Luetin reaction in syphilis (abstr.), 359
Lupus erythematosus, acute, with nodular necrotic cutaneous tuberculides of arms and hands, feet and legs (Eddowes), 142
— — nodular, followed by atrophy of the skin and subcutaneous tissue (MacLeod), 136
— vulgaris, multiform, following measles (Pernet), 326
— — of leg, extensive exuberant, originating from a tuberculous abscess (Pernet), 326
— — radium treatment of (Haslund), 294
Lymphangitis ?, case of (Corbett), 250

Malignant ulceration of the skin, secondary, case of (Dore), 344
Mange from the kitten, pruritic dermatitis caused by infection of (Whitfield), 337
Mercury, a study of the comparative toxity of the various preparations of (abstr.), 81
— in Verrucæ planæ juveniles, use of (abstr.), 78, 152
Molluscum fibrosum and dermatolysis, with congenital morbus cordis and kyphosis (Sequeira), 69, 147
Monilothrix (abstr.), 352
Morphœa, case of circumscribed sclerodermia in a child (Stowers), 343
Morphœo-sclerodermia, case of, with recent acute symmetrical involvement of the soles of the feet (Pernet), 49
Muscles of the skin of the chin, the smooth (abstr.), 345
Myasis, cutaneous, in man (abstr.), 347
Mycosis fungoides in a woman (Pringle), 246
Myxœdema, sclerodermia associated with Graves's disease and later (Little), 124
— sclerodermia occurring in a case of (Sequeira), 46

Nævus anæmicus (abstr.), 346
— an unusual case of extensive pigmented hairy (Pernet), 122
Nails, dystrophy of, in malaria (abstr.), 352
Necrosis of skin from handling "composition" (an explosive) (MacLeod), 135
Neisser, Albert: Obituary, 320
Neo-salvarsan and salvarsan, the fixation of, by the blood after intravenous injection (abstr.), 157
— or salvarsan, on the bactericidal power acquired by the serum after administration of (abstr.), 83

Occupational dermatoses (abstr.), 76
— — necrosis of skin from handling "composition" (an explosive) (MacLeod), 135
Oriental sore, case of, treated by antimonium tartaratum (tartar emetic) locally (abstr.), 75

Papilliferous sudoriparous cyst of the cheek in a man (Little), 269
Papillomatosis, chronic diffuse, of the left foot and leg (Little), 140
Parakeratosis variegata of the type described by Juliusberg as "Pityriasis lichenoides chronica" (Little), 239
Pityriasis lichenoides chronica (Juliusberg) (Little), 239
— rubra pilaris (Sibley), 261
Porokeratosis, a peculiar form of (abstr), 354
"Porokeratosis Mibelli," contribution to the histology of the so-called (abstr.), 353
Pre-cancerous dermatosis (abstr.), 77
Protozoal diseases, treatment by tartar emetic, alone or in combination (abstr.), 353
Pruritic dermatitis caused by infection of mange from a kitten, cases of (Whitfield), 337

Psoriasis as a sequel to acute inflammation of the tonsils (abstr.), 273
— auto serum therapy in (abstr.), 354
Pudenda, ulcerating granuloma of, the treatment of (abstr.), 75
Purpura annularis telangiectodes (Majocchi) (abstr.), 351

Quarterly Survey of Dermatological Literature, 84, 163, 278, 363

Radium efficiency in non-malignant surgical conditions (abstr.), 355
— extensive carcinoma of face ocurring in the course of a Kerodermia pigmentosa, treated by a massive dose of (Pringle), 253
— treatment of Lupus vulgaris (Haslund), 294
Report of Royal Commission on Venereal Diseases (Editorial), 229
— the Fourteenth Annual, of the Institute for Medical Research, Kuala Lumpur, 1914, 70
Reviews:
  The Medical Annual, 1916, 171
  The Mortality from Cancer throughout the World (Hoffman), 171
  The Pathology of Tumours (Kettle), 171
Ringworm of the scalp in Sydney, the occurrence of (abstr.), 151
— in the Province of Naples (abstr.), 361
Roentgen deep therapy in malignant tumours (abstr.), 355
Royal Society of Medicine (Dermatological Section), 40, 124, 239, 321

Salvarsan and neosalvarsan, the fixation of, by the blood after intravenous injection (abstr.), 157
— ("606") in concentrated solutions (abstr.), 161
— in primary syphilis, five years' experience with "606" (abstr.), 82
— or neosalvarsan, on the bactericidal power acquired by the serum after the administration of (abstr.), 83
— the toxicology of (abstr), 158
Sarcoma, idiopathic multiple pigment (Kaposi), case of so-called (Weber), 64
— Kaposi's multiple pigmentary (Sibley), 333
— multiple idiopathic hæmorrhagic (Kaposi), three cases of so-called (Weber), 319
Scabies, treatment of, by sulphur vapour (abstr.), 351
Schamberg's disease (Adamson), 334
Sclerodactylia, diffuse sclerodermia with (Bunch), 145
Sclerodermia associated with Graves's disease and later myxœdema, benefiting conspicuously by implantation of human thyroid into the bone marrow (Little), 124
— circumscribed (morphœa), in a child (Stowers), 343
— diffuse, with sclerodactylia (Bunch), 145
— four cases of, associated with disease of the thyroid gland (Sequeira), 31
— morphœo-, case of, with recent acute symmetrical involvement of the soles of the feet (Pernet), 49
— occurring in a case of myxœdema while under thyroid treatment (Sequeira), 46
— with Graves's disease (Sequeira), 69
Sebaceous adenoma (Pringle type) in mother and daughter (Sequeira), 340
Simpson arc lamp, some experiments with (abstr.), 80
— light; its nature, mode of production, and application (abstr.), 79
Spectrum, from the visible to the Gamma ray (abstr.), 78
Spirochætes and their granule phase (abstr.), 155
Sprays and spraying in the treatment of certain surface affections of the skin (Jamieson), 104
Staphylococcia in a xerodermatous patient (Pernet), 138
Streptococcal necrosis, acute, of skin and subcutaneous tissues (MacCormac), 318

Sugar-content of the blood in various diseases of the skin (abstr.), 153
Sulphur vapour, treatment of scabies by (abstr.), 351
Sweating of the face, case of localised, and (?) hidrocystoma (Dore), 343
Syphilide, recurrent, simulating reinfection (Spence), 143
— tertiary (Ward), 65
Syphilis, a family of occult (abstr.), 157
— a new test for (the emulsoid-gelation, or the "Gel" test) (McDonagh), 114, 249
— a new remedy for, Luargol or 102 (abstr.), 357
— and yaws in the Tropics (abstr.), 156
— in the Army, the treatment of: with special reference to the administration of "606" in concentrated solutions (abstr.), 161
— luetin reaction in (abstr.), 359
— primary, on the gums (abstr.), 356
— — salvarsan in; five years' experience with "606" (abstr.), 82
— tertiary, treated by intramine (Pernet), 245
— the pathology of (abstr.), 81
— the principles of the treatment of (abstr.), 356
— treated by "intramine" (McDonagh and Spence), 53
Syphilitic analgesia, a case of Fournier's secondary (Rasch), 119
— chancre, primary, of the lip (Pernet), 139
Syphilitics, presence of different antibodies in the serum of (abstr.), 358
Syringoma, a case of (Paul and Adamson), 106

Tartar emetic, case of Oriental sore treated by (abstr.), 75
— — successful treatment of ulcerative Granuloma pudendi by means of (abstr.), 149
— — the treatment of certain diseases of protozoal origin with (abstr.), 353
Telangiectasia hereditaria hæmorrhagica (Osler) (abstr.), 151
Tetryl dermatitis, the prevention, symptoms, and treatment of (abstr.), 148
Thyroid gland, four cases of sclerodermia associated with disease of (Sequeira), 31
Tinea circinata of tropical origin, a case of very extensive (Little), 57
Trefoil dermatitis or the sensitisation of unpigmented skin to the sun's rays by ingestion of trefoil (abstr.), 274
Trichophytides, secondary lichenoid, in association with Kerion Celsi (Rasch), 9
Trichophyton violaceum, pseudo-actinomycotic formations produced experimentally with (abst.), 361
Tuberculosis cutis, acute disseminated (Little), 243
Tuberculous disease of the face, case of, (Stowers), 323
Tumours of the skin, very unusual (Little), 146

Ulcerating granuloma of the pudenda, the treatment of (abstr.), 75
— — successfully treated by injections of antimony (abstr.), 352
Ulcerative granuloma pudendi, notes on the successful treatment of, by means of tartar emetic (abstr.), 149
Ulceration, chronic (Little), 58
Urticaria pigmentosa, congenital (Pernet), 254
— — in an adult (Little), 327
— — ? in a soldier, aged 19 years (Sibley), 327
Urticarial and erythematous eruptions resulting from sensitisation to certain foods (abstr.), 153

Varicella-like spots, generalised eruption of, two cases of Herpes zoster associated with (Weber), 13
Venereal disease in the Army, the treatment of (abstr.), 160
— diseases, Report of Royal Commission on (editorial), 229

Verrucæ planæ juveniles, use of mercury in (abstr.), 78, 152

White, James Clarke, "In Memoriam" (Morris), 1

Xanthoma tuberosum (Little), 321
Xerodermatous patient, Staphylococcia in (Pernet), 138
Xerodermia pigmentosa, extensive carcinoma of the face occurring in the course of, treated by a massive dose of radium (Pringle), 253
X-ray burn, general carcinomatous infiltration of skin of arm apparently resulting from (Little), 129

Yaws and syphilis in the tropics (abstr.), 156

INDEX OF NAMES

OF EXHIBITORS OF CASES AND AUTHORS OF ORIGINAL ARTICLES.

Adamson, H. G., 27, 106, 135, 281, 334, 337

Bunch, J. L., 145

Corbett, Dudley, 250, 251

Dore, S. E., 66, 133, 343, 344

Eddowes, Alfred, 53, 142, 268

Gray, A. M. H., 46

Haslund, P., 294
Hayne, P. A., 255

Jamieson, W. A., 104

Little, E. Graham, 40, 41, 57, 58, 63, 124, 129, 140, 146, 239, 242, 243, 255, 263, 269, 321, 327

MacCormac, H., 318
McDonagh, J. E. R., 53, 114, 173, 207, 259
MacLeod, J. M. H., 135, 136
Morris, Sir Malcolm, 1

Paul, S. Norman, 106
Pernet, George, 49, 122, 136, 138, 139 245, 254, 317, 325, 326, 342
Pringle, J. J., 246, 253

Rasch, C., 9, 119
Rolleston, J. D., 110

Samuel, H. C., 266
Sequeira, J. H., 31, 46, 69, 147, 254, 339, 340
Sibley, W. Knowsley, 42, 51, 131, 261 327, 329, 333, 341
Spence, H., 53, 143
Stowers, J. H., 323, 343

Trotter, Wilfrid, 46

Ward, Gordon, 65
Weber, F. Parkes, 13, 64, 309, 343
Whitfield, A., 337

Nos. 327-9.—Vol. XXVIII, Nos. 1-3.] [JAN.-MARCH, 1916.

THE BRITISH JOURNAL OF DERMATOLOGY

SUMMARY OF CONTENTS.

PAGE

In Memoriam: James Clarke White. Sir MALCOLM MORRIS, K.C.V.O. 1

Clinical Note. Secondary Lichenoid Trichophytides in Association with Kerion Celsi (Lichen Spinulosus Trichophyticus). C. RASCH, (Translated from the Danish by W. Jenkins Oliver) 9

Two Cases of Herpes Zoster associated with a Generalised Eruption of Varicella-like Spots: One of the Cases followed by Oculomotor Paresis, Mydriasis, and Frontal Anæsthesia. F. PARKES WEBER, M.D., F.R.C.P. 13

Specific Hypersensitiveness or Allergy in Relation to Certain Eruptions of Microbic Origin. H. G. ADAMSON, M.D.Lond. 27

Four Cases of Sclerodermia associated with Disease of the Thyroid Gland. J. H. SEQUEIRA, M.D., F.R.C.P., F.R.C.S. . 31

Royal Society of Medicine.—Dermatological Section . . 40

The Fourteenth Annual Report of the Institute for Medical Research, Kuala Lumpar, Federated Malay States, 1914 . 70

Current Literature 73

Quarterly Survey of Dermatological Literature 84

Personal Note.—Deaths.—Announcement 92

For Full Contents see page ii.

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